# AUTOLOGOUS BONE MARROW TRANSPLANTATION AS A MEANS OF INTENSIFYING THE TREATMENT OF PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES.

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The following thesis contains information from many patients collected over a period of years. It represents the combined efforts of a dedicated team of doctors, nurses and other colleagues who have contributed to the care of the patients and without whom this thesis would not have been possible.

I was appointed as Senior Registrar in Haematology, in May 1980, and I have been closely involved with the autologous bone marrow transplant programme at University College Hospital, London, since then. I was a member of the original group who following lengthy discussions proposed the early treatment protocols.

I have been a member of the team looking after the day to day care of the autograft patients, particularly the early patients. I have reviewed the notes of all patients whom I was not personally involved in the care of. I have acted as transplant co-ordinator throughout this period.

I have been solely responsible for collecting and tabulating the data. Where patients were treated outside of University College Hospital, I have visited to collect data or discuss the patients with their supervising clinician.

It is because of my familiarity with the patients and their data, that I have been able to make various observations, identifying for example, the differences in infective morbidity between patients with AML and ALL, and the likely importance of the time to achieve CR1 as a

prognostic indicator in patients with AML treated during first remission and finally to suggest future treatment protocols based on the present results.

## ABSTRACT

The aim of this thesis is to assess the feasibility of using autologous bone marrow transplantation (ABMT), to allow escalation of the dose of cytotoxic agents which may successfully be employed to increase the response rate and prolong the disease free survival in patients with acute leukaemia or relapsed lymphoma.
A total of 78 patients have been treated with a variety of intensive chemoradiotherapy regimens followed by ABMT. There have been 12 (15%) procedure related deaths.

Acute Myeloid Leukaemia (AML) - Patients treated in first remission: 10 (62.5%) of 16 patients remain in 1st remission with a median follow-up of 24 months (range 16-61) post ABMT. The six relapses that occurred were between 1-15 months post ABMT.

Acute Lymphoblastic Leukaemia (ALL) - Patients treated in first remission: Only one of eight patients treated (12.5%) remains in remission 34 months post ABMT. Three patients died during the procedure. Four patients relapsed; 2, 11, 32 and 33 months post ABMT.

AML & ALL - Patients treated at a later stage: 18 patients were treated either at relapse or during a later remission, only 2 patients, both with ALL, remain alive

in remission, 22 and 48 months post ABMT. Two patients died procedural deaths. Fourteen patients relapsed and died, 2-13 months post ABMT.

Non-Hodgkin's Lymphoma: 21 patients have been treated, 8 achieved a complete remission (CR), 3 a partial remission (PR), 6 had no response and four were not evaluable because of early deaths. Only 3 patients remain in remission at 7, 6, and 6 months post ABMT without further treatment. Three further patients have received additional radiotherapy since their ABMT and one chemotherapy as well, they are now in remission 42, 32 and 29 months post ABMT.

Hodgkin's Disease: 15 patients were treated, 11 achieved a CR, 3 a PR but only 4 remain in CCR 29, 17, 8, and 7 months post ABMT. One patient died an early death and was not evaluable.

CONCLUSIONS:

(1) The use of intensive chemoradiotherapy followed by ABMT is feasible in these groups of patients, even though many have received extensive prior therapy and some have been in poor clinical condition at the time of ABMT.

(2) The response rate has been high, even where disease was thought to be resistant to conventional doses of cytotoxic agents. Some of these responses have been well maintained.

(3) Intensive chemoradiotherapy with ABMT should now be considered earlier in the course of most of these diseases when treatment related complications should be less.

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# CHAPTER 1

## INTRODUCTION

The aim of this thesis is: 1) to assess the feasibility of using high dose chemoradiotherapy regimes followed by autologous bone marrow transplantation (ABMT) to ameliorate the severe marrow toxicity thus produced, in patients with leukaemia and lymphoma, 2) to evaluate the results in terms of response rate and long-term disease free survival (DFS) in these patients and finally 3) to consider the results in the context of other currently employed regimens with a view to suggesting future protocols.

### WHY USE BONE MARROW TRANSPLANTATION ?

The haematological malignancies were once a group of incurable diseases. Over recent years treatment regimens have been increasingly successful at producing complete remissions (CR), extended disease free survival (DFS) and even cure in some patients with these diseases.

The early use of cytotoxic drugs was with single agents and as the diseases were regarded as incurable, most were used only in an attempt at palliation. It was

however, soon noted that a better response was often produced by a higher dose of the agent employed (eg nitrogen mustard, Brindley et al, 1964)[24]. This was in keeping with the evidence that there was a definite dose-response curve in the use of radiotherapy to treat localized Hodgkin's Disease (HD) (Kaplan HS, 1962)[99].

The awareness of a relationship between dose and response resulted in escalation of the doses of cytotoxic agents employed but this also led to increased toxicity. Drug combinations were a way of attempting additive antitumour effect whilst minimising the toxicity to the patient. The improved results in patients with HD as reported by DeVita et al, 1965[49], with MOPP, demonstrated the effectiveness of this approach. In sensitive tumours there is a steep dose-response curve for radiotherapy, however, the amount of total body irradiation (TBI) which can be tolerated by the patient is limited by myelosuppression. If myelosuppression can be circumvented, then the amount of TBI is limited by toxicity to other organs.

In an attempt to increase the tumoricidal effect, supra-lethal doses of TBI have been given successfully to patients, by using syngeneic, allogeneic or rarely autologous bone marrow transplantation to rescue them from the otherwise fatal myelosuppression.

The rationale for this form of dose escalation supposes that there is a steep dose-response curve for the therapeutic modality employed. Animal experiments have demonstrated that such dose-response curves do exist (Bruce et al, 1966; Frei & Canellos, 1980)[26,69]. In humans the best demonstration of a dose-response curve is the eradication of leukaemia by TBI and cyclophosphamide (Thomas et al, 1979)[173]. The major dose limiting factor for an agent or combination of agents, is the toxicity produced. Where the major toxicity is myelosuppression, then the use of allogeneic, syngeneic or autologous bone marrow transplantation (ABMT) will allow dose escalation and thereby an improved response rate.

There will be few patients who have an identical twin, therefore syngeneic transplantation is not an available alternative for most patients. If the use of allogeneic and autologous marrow was associated with the same toxicities then allografting might be considered preferable to autografting as there would be no risk of contamination of the marrow with clonogenic tumour cells.

## WHAT LIMITS ALLOGENEIC BONE MARROW TRANSPLANTATION ?

Allogeneic transplantation was first employed in patients with acute leukaemia in the late 1950's and early 1960's.

In 1963 Mathe et al[116], were the first to report long-term survival and evidence of engraftment in a 26 year old patient who was given an allogeneic graft after conditioning with methyl-nitro-imidazolyl-mercaptopurine and TBI for the treatment of resistant relapsed leukaemia. He suffered acute graft-versus-host disease (GVHD) and later chronic GVHD and died leukaemia free at 20 months of varicella encephalitis.

Since that time allogeneic transplantation techniques have continued to develop and at the present time allogeneic transplantation is the recommended treatment for young patients with acute leukaemia who have relapsed and is possibly also the treatment of choice for young patients with acute myeloid leukaemia (AML) in first CR (Gale & Champlin 1986)[71]. Patients must usually be under 40 years of age and have an HLA (Human Leucocyte Antigen) identical sibling for the marrow donor. Younger patients do best with a 75% long-term survival for those patients less than 20 years of age and only 25% for those over 30 years old. This is due to an increase in deaths from pneumonitis and GVHD in the older age group and not to relapse of their disease (Thomas ED, 1983)[168].

Current research is directed to trying to eliminate these treatment related complications. A variety of radiation schedules have been used to try and reduce the radiation induced pneumonitis (Buckner at al, 1982)[28].

GVHD is often found in association with pneumonitis. Its onset in a particular patient is unpredictable but acute GVHD is more common in the older patient.

During the early years of experimental marrow transplantation, the ultimate fate of animals surviving received little attention. The first report of secondary mortality was made by Barnes & Loutit, 1955[12]. The authors reported that lethally irradiated CBA mice that received syngeneic spleen cells were all afforded long-lasting protection but that nine out of 16 lethally irradiated CBA mice that received spleen cells of strain A mice although surviving for 30 days, died before 100 days after transplantation. These observations were soon confirmed by many other workers. Cohen et al, 1957[44], drew attention to the severe diarrhoea, weight loss and skin lesions that occur in animals during the period of delayed mortality. Over the next few years observations of a number of laboratories suggested that 'secondary disease' was in fact graft-versus-host disease (GVHD)(van Bekkum & de Vries, 1967)[178]. This concept was further strengthened by the observations of Billingham & Brent, 1957[17], who observed a runting syndrome in newborn mice that had been transplanted with allogeneic spleen cells. The main observations in 'runt disease' were retarded growth and development, diarrhoea, varying degrees of hypoplasia of the lymphatic system, skin lesions and focal necrosis of the liver cells. Every one of these

observations was also made in animals given allogeneic marrow transplants following lethal TBI. Perhaps the most convincing pieces of evidence that supported a graft-versus-host mechanism in radiation chimeras was the observation that on increasing the number of lymphoid cells injected together with the marrow, the severity of the secondary disease could be increased and the delay between transplantation and appearance of signs of the disease could be reduced (Santos & Cole, 1958; van Bekkum & de Vries, 1967)[153,178]. It soon became apparent to most workers that the cell initiating GVHD was a lymphocyte (Grebe & Streilein, 1976)[83].

Billingham (1966-67)[16] stated that the essential requirements for GVHD were: "(1) The graft must contain immunologically competent cells; (2) The host must possess important transplantation isoantigens that are lacking in the graft donor, so that the host appears foreign to it, and is therefore, capable of stimulating it antigenically; (3) The host itself must be incapable of mounting an effective immunological reaction against the graft, at least for sufficient time for the latter to manifest its immunological capabilities i.e., must have security of tenure." The three important target organs in man are skin, gut and liver (van Bekkum & de Vries, 1967)[178].

The Seattle group demonstrated that the prophylactic

use of methotrexate could markedly reduce GVHD in lethally irradiated dogs given allogeneic but major histocompatibility complex (MHC) - matched bone marrow (Thomas et al, 1963; Storb et al, 1970)[170,163]. They adopted the use of methotrexate for prevention of GVHD in clinical studies in man and, except for the Baltimore group who demonstrated a similar effect for the use of cyclophosphamide in rodents and primates (Santos & Owens, 1966; Owens & Santos, 1971)[154,125] methotrexate was the standard agent initially adopted for the prevention of GVHD in all centres.

It was hoped that the introduction of cyclosporin A, a cyclic polypeptide with immunosuppressive properties, would prevent or reduce acute GVHD. Animal studies suggest that cyclosporin A inhibits the development of cell-mediated reactions by blocking resting lymphocytes. It also inhibits production of lymphokines. It would appear that cyclosporin A will reduce the severity of acute GVHD but not its incidence or its influence on overall survival (Powles et al, 1980; Deeg et al, 1985)[132,47]. Seattle have now reported a study comparing the use of a combination of both methotrexate and cyclosporin with cyclosporin alone to prevent acute GVHD. The combination appears to be better than cyclosporin alone and may improve survival (Storb et al, 1986)[164].

Current attempts to reduce acute GVHD by eliminating T

cells from the donor marrow and thereby extending the use of allogeneic marrow, are undergoing clinical trials (Prentice et al, 1984)[134]. Whilst this technique appears useful at reducing the incidence of acute GVHD it does not eliminate it completely and whether it improves overall survival remains to be seen.

The conditioning regimen used for allogeneic bone marrow transplantation in acute leukaemia has two functions: firstly to serve as immunosuppressive therapy to prevent rejection of the allogeneic marrow and secondly to eradicate host disease. The conditioning regimen most commonly used is TBI given as a single dose or in fractions to a total dose of 9-12 Grays together with cyclophosphamide 60 mg/kg on two consecutive days, as pioneered by the Seattle transplant team (Thomas et al, 1975)[171]. Rejecton of a marrow graft following this regimen in patients allografted for acute leukaemia is rare.

Relapse still remains a problem. In patients with AML treated by allograftiing in first CR the incidence of relapse is reported to be between 10 and 25% (O'Reilly RJ, 1983; Deeg et al, 1984)[124,46]. The majority of relapses occurring in the first two years post graft, although relapse has been reported even six years later (Deeg et al, 1984)[46]. Fewer patients with acute lymphoblastic leukaemia (ALL) have been allografted in

first CR but relapse appears more frequent than in patients with AML. In patients with AML and ALL allografted after first CR the relapse rate is higher (Appelbaum et al, 1983; Deeg et al, 1984)[8,46] with five year survival of less than 27% in ALL with leukaemic relapse being the commonest cause of death (Thomas et al, 1983)[175].

In the first 100 patients transplanted in Seattle for acute leukaemia in relapse, a time at which the leukaemic burden would be high and the disease is more likely to be resistant than early in first CR, the majority of patients surviving the procedure relapsed (Thomas et al, 1977)[172]. Twelve patients not only achieved a CR but remain in remission many years later (Thomas ED, 1983)[168]. This approach is therefore capable of eradicating disease in a small proportion of patients with relapse but there is no way of knowing in advance which patients will be cured and which will relapse again.

SYNGENEIC BMT

Thomas et al, 1975[171], reported the use of syngeneic or monozygotic twin marrow to rescue leukaemic patients with advanced disease following lethal doses of TBI. There is no risk of GVHD following syngeneic grafts and

therefore no immunosuppressive therapy is required to prevent rejection of the graft. This study demonstrated a definite antileukaemic effect of the TBI, however, all patients relapsed again within 12 weeks, demonstrating the need for a more powerful antileukaemic conditioning regimen.

Syngeneic grafts treated with the same conditioning regimen as allografts have no GVHD and immediate survival is greater, but leukaemic relapse is also greater (Fefer et al, 1981)[62]. There is some evidence that a graft-versus-leukaemia (GVL) effect may operate when GVHD is present (Weiden et al, 1979, 1981)[181,182,183]. However, other observations do not support the existence of an allogeneic GVL effect. There is no difference in the relapse rate after allogeneic BMT for chronic granulocytic leukaemia (CGL) in chronic phase, compared to that after syngeneic BMT (Fefer et al, 1985; Thomas et al, 1985)[64,176] neither is there any correlation between GVHD and post transplant relapse rate for patients with AML transplanted with allogeneic marrow in CR1 or for chronic phase CGL (Fefer 1986)[61]. Furthermore, attempts to manipulate GVHD to increase its incidence and severity has not improved leukaemic relapse rate (Sullivan et al, 1984)[166]. The strongest circumstantial evidence correlating GVHD and a GVL effect is restricted to children transplanted with allogeneic marrow for ALL in relapse (Sanders et al, 1985)[150].

Autologous marrow has been used since the 1950's to allow dose escalation above the accepted maximum dose of the agent employed (whether chemotherapy or irradiation) in an effort to obtain better responses in solid tumours. The intention was not to rescue the patient from marrow ablation but rather to speed haematological recovery.

Clifford et al, 1961[43], gave autologous marrow infusions to 3 patients following high doses of nitrogen mustard used in the treatment of head and neck tumours. 6 patients received the highest dose, 3 of these were followed by an infusion of autologous marrow. The 3 patients who received autologous marrow survived, whilst the remaining 3 died before regeneration. The authors concluded patients could survive high dose nitrogen mustard therapy if accompanied by an infusion of autologous marrow.

Pegg et al, 1962[126], used autologous marrow infusions after varying amounts of wide-field or total body irradiation and also differing chemotherapeutic agents, in 23 patients with a variety of advanced malignant diseases. They concluded that the rapidity of haematological recovery was increased after some of the agents but not others.

Although these and other studies demonstrated the feasibility of using autologous marrow in humans, the neoplastic disorders treated were generally only palliated and overall survival was not improved.

It is only since allogeneic transplantation following TBI and cyclophosphamide has been demonstrated to produce cures in some patients with end-stage leukaemia (Thomas et al, 1977)[172] that there has been revived interest in the use of autologous transplantation in the haematological malignancies.

Autografts are similar to syngeneic grafts in that they do not cause GVHD, autografting can therefore, be safely used in older patients and an HLA identical sibling is not required. It is therefore, a technique which is likely to be applicable to a much wider group of patients. It is unlikely, as there is no GVHD, that there will be a GVL effect. Fefer, has suggested however, that ABMT may be preferable to syngeneic grafting as the autologous marrow having been exposed to the tumour, might have become primed to putative tumour associated antigens, and might therefore, exert an anti-tumour effect when reinfused (Fefer 1986)[61]. Many murine models have been established in which disseminated leukaemia or lymphoma can be cured by a combination of non-curative chemotherapy and infusion of syngeneic T cells immune to the tumour (Fefer et al, 1982)[63].

It would seem reasonable to assume that as with syngeneic grafts there may be a need for a greater anti-leukaemic effect from the conditioning regimen pre-ABMT.

Autologous or syngeneic bone marrow grafting has the advantage that immune mediated graft rejection does not occur. The autologous bone marrow must however, be assumed to be contaminated with residual leukaemia in view of the relapsing nature of the disease.

With the successful use of intensive chemoradiotherapy followed by allografting in patients with acute leukaemia consideration of intensifying the treatment of patients with poor prognosis lymphomas by allografting has also received attention. The difficulty is to decide which patients are likely to benefit from transplantation at an early stage of their disease. Poor prognostic indicators are becoming increasingly recognised but most of the patients with non-Hodgkin's lymphoma (NHL) will be more than 40 years of age. The patients with HD who are going to do badly may not be recognised until they have had many prior treatment regimens when their disease is unlikely to be cured by any currently employed conditioning regimens.

There would appear to be two main problems to consider when deciding on a suitable conditioning regimen for ABMT in the haematological malignancies: the eradication of

disease in the patient as in the allograft situation and the eradication of potential residual disease in the autologous marrow. This is discussed in the following chapters relating to the individual diseases.

# CHAPTER 2

## PATIENTS AND METHODS

### PATIENTS

All adult patients with acute leukaemia or advanced relapsed lymphoma were considered eligible for intensive chemoradiotherapy regimens with ABMT rescue. Other significant medical conditions were regarded as a relative contraindication and patients were rejected only if it was thought likely it would affect the safe outcome of the procedure. The criteria for each condition are discussed later.

### BONE MARROW HARVESTING

Bone marrow was harvested if judged clear of disease by morphological examination under the light microscope, of aspirates in all patients, and trephine biopsies as well in lymphoma patients.

Bone marrow was harvested by aspiration from the posterior and anterior iliac crests and where necessary from the sternum during a general anaesthetic. Klima bone marrow needles were used. Initially 2-4 ml aliquots only were aspirated from each site. However, in a local study

where one operator aspirated 2-4 ml aliquots and the other operator 5-12 ml aliquots, we were unable to demonstrate a significant difference in the nucleated cell count thus obtained and we now aspirate up to 12 mls from each site. The needles and syringes are flushed out before each aspiration with preservative free heparin. Each aliquot is then transferred by injecting directly, without filtering, into a two-litre transfer pack containing 200 mls of tissue culture medium (TC 199 Gibco Europe) with 8000 units of preservative free heparin.

The aim was to harvest a minimum of $2x10^8$ cells/kg body weight. It was found, however, that any gain in nucleated cells obtained in a volume exceeding 1,000 mls was lost during later processing and that the optimum volume of marrow to be harvested was around 800 mls. If $<1.0x10^8$ cells/kg is now obtained after final processing a second harvest is planned before proceeding to ABMT.

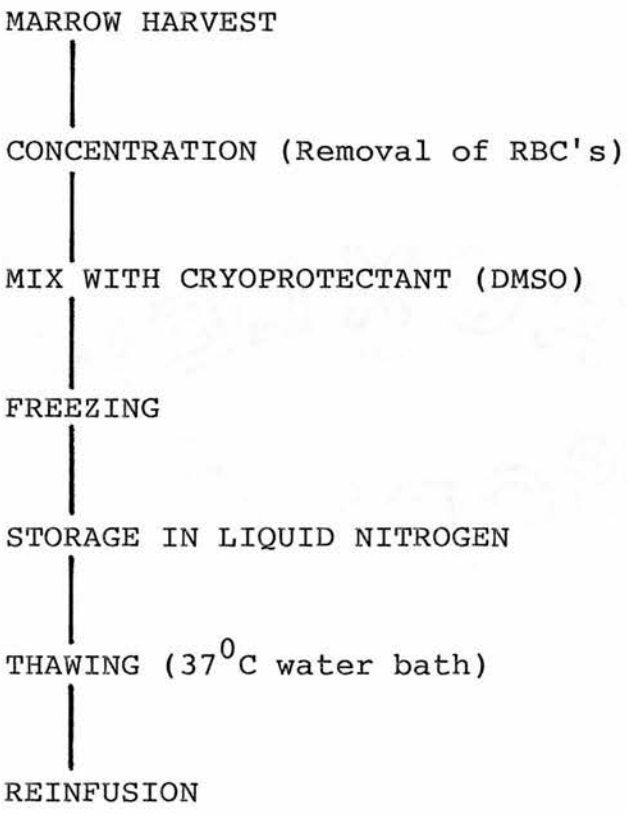



Figure 1. Schematic representation of 'ex vivo' autologous marrow processing.

MARROW PROCESSING

To concentrate the marrow we use a Hemonetics model 30 cell separator. This is set up using a paediatric pheresis pack as for a conventional leucopheresis. As the marrow is already anticoagulated with heparin the anticoagulant line on the harness is clipped off. The draw needle adaptor is also clipped off and the marrow enters the system through the saline reinfusion female connector via a conventional drip set. The filter in this

drip set prevents small clots frequently present in the harvested marrow from entering the system. The bowl is then filled at a rate of approximately 100 ml/min. When the buffy coat reaches the top of the bowl the filling rate is reduced to 20 ml/min and the buffy coat redirected through the white cell collection port into a 600 ml transfer pack. Collection is usually continued for two minutes. The aim of processing is to end with a predetermined volume of buffy coat (250 ml) in the transfer bag for freezing. Once all the marrow has been processed the drip set is transferred to the reinfusion bag port allowing the red cell and plasma discard to be reprocessed, extracting the last vestiges of buffy coat until the desired volume is obtained. For efficient processing of marrow using the intermittent flow cell separator the total volume of red cell discard must fill the bowl (i.e. 100 ml) as this is used to displace the buffy coat. This method of marrow processing removes most of the red cells prior to freezing and thawing.

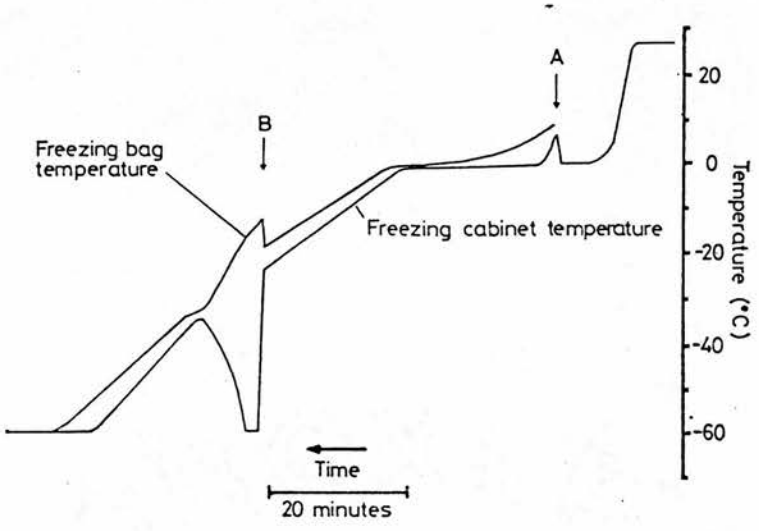
MARROW FREEZING

The volume of the processed marrow is determined by weight and an equal volume of precooled 20% (vol/vol) dimethyl sulphoxide (DMSO Analar grade) in TC 199 is added via a transfer set and three-way tap using a 50 ml disposable syringe. This addition is performed in a ten minute period with good mixing to minimise osmotic shock. This procedure is performed on ice in a laminar flow sterile hood. Equal volumes (100-150 ml) of the processed marrow and cryopreservative are then transferred via a second transfer set attached to the three-way tap into four 700 ml Gambro Hemofreeze bags (DF-700-3). Ten to twenty millilitres are also placed in 2 ml freezing vials to enable repeated evaluation of the freezing and storage. Previous studies with peripheral blood leucocytes from patients with chronic granulocytic leukaemia showed that the progenitor cell recovery from both the 2 ml vial and the 120 ml bag were very similar when both were frozen at the same time. The four Hemofreeze bags are sandwiched between aluminium plates and placed with the vials in a Cryoson BV-4 biological freezer (Cryotech Ltd. UK). A thermocouple placed against one of the bags gives a continuous reading of the bag temperature and another thermocouple within the freezing cabinet gives a continuous reading of the cabinet temperature. The samples are allowed to equilibrate at $0^{o}C$ for approximately 10 min and the cabinet is then

cooled at 1.2°C per minute until the liquid to solid phase change. This is indicated by the rise in the bag temperature due to the release of the latent heat of fusion. At this stage the cabinet temperature is dropped rapidly by a manual override to -60°C to minimise the post-freezing plateau (Figure 2). When the latent heat release is over, the cabinet temperature is allowed to rise to -35°C and the cabinet is then cooled 2.0°C per minute, during which time the freezing bag cools at about 1.25°C per minute. This cooling rate is then maintained to -60°C at which stage the bags and vials are transferred immediately into liquid nitrogen where they are stored until used. Similar freezing regimes have been used by others (Lewis et al, 1967; Wells et al, 1979)[105,186].

The 2 ml vials containing aliquots of every marrow harvested are stored separately to allow 'in vitro' assessment of Gm CFC as part of the routine evaluation of our cryopreservation technique.

Further discussion of the technique for harvesting and cryopreservation has already been published (Linch et al, 1982)[107].




Representative cabinet and freezing bag temperature recordings are shown.

A = freezing bags and 2 ml vials placed in precooled freezing cabinet.

B = phase change with latent heat release.

Figure 2. Cryopreservation of bone marrow: freezing curves.

MARROW THAWING AND REINFUSION

The bags of frozen marrow are transported to the bedside in a portable liquid nitrogen container. The bags are then rapidly thawed, one at a time, by immersion in a water bath (37$^{o}$C). The marrow is then infused without washing through a blood giving set into a central line, each bag being infused over about 10 minutes. Each patient is given 10 mg of chlorpheniramine intravenously, immediately prior to marrow infusion. The only problems attributable to the DMSO infused have been that of its unsavoury taste and smell and minor febrile reactions. One patient collapsed at the time of marrow infusion with rapid recovery. The cause was never ascertained.

The amount of free haemoglobin transfused is small, but patients and staff are warned to expect apparent haematuria and a high fluid input is maintained immediately post marrow infusion.

ASSESSMENT OF HAEMATOLOGICAL RECOVERY

Blood samples from all patients were evaluated for haematological recovery on a Coulter S Plus. Automated cytochemistry was also performed on a Hemalog D90. Patients included early in the study had fewer Hemalog D counts but efforts were made to obtain daily counts in the later patients during the early regenerative period.

The principles of the Hemalog D90 have been previously described (Ansley & Orstein, 1970; Mansberg et al, 1974)[4,112]. One component of this automated differential white cell count is an electronic threshold area into which large cells having no cytochemical staining are counted. This group of large unstained cells (LUC's) is usually considered to be part of the lymphocyte population if it falls within the normal range (0.8-3.1%). However, when this cell component is elevated immature cell types and atypical lymphoid cells must be considered and a May-Grunwald Giemsa stained blood film examined.

The high level of precision of the differential white cell count in leucopenic patients using this technique has previously been reported (Ross & Bardwell, 1982)[147]. In leucopenic patients with an absolute neutrophil count of $0.5 \times 10^9$/L the co-efficient of variation is 8% compared to a 20% co-efficient of variation using manual methods

of differential white cell counting.

During the course of this study it was observed that blood samples run on the Hemalog D90 often had a high percentage of LUC's in the period immediately prior to a detectable return of the total WBC count on a Coulter counter. This is discussed further in Chapter 7: Haematological Recovery.

## NURSING PRECAUTIONS

All patients receiving very high dose chemoradiotherapy regimens were nursed in single rooms without filtered air precautions. The patients were reverse barrier nursed while their neutrophil count was below $0.5x10^9/L$.

## VENOUS ACCESS

All had Hickman central catheters inserted by the surgical team whilst under a general anaesthetic prior to starting chemotherapy.

## CLINICAL MANAGEMENT

### Pre-ABMT

Each patient had a full physical examination by myself or another member of the transplant team, a chest X-ray (CXR) and electro-cardiograph (ECG). In the latter part of the study a radionuclide ventriculogram was also performed if substantial amounts of cardiotoxic drugs, particularly anthracyclines had already been given. A full blood count (FBC), biochemical screen* and a full microbiological screen** were assessed prior to starting the conditioning regimen.

* Biochemical screen: blood urea, electrolytes, creatinine, uric acid and liver function tests.

** Microbiological screen: A skin swab taken from the Hickman exit site, a throat swab, a mid stream urine sample and faeces were cultured to obtain sensitivities of any potential pathogen, together with a blood sample to detect the presence of hepatitis B surface antigen (HBsAg).

Remission patients: Patients with acute leukaemia in remission were treated with the high dose chemotherapy regimen as an elective procedure. The treatment was discussed with the patient and offered as an alternative to conventional chemotherapy. At least two patients, one with AML and one with ALL, chose to have conventional treatment.

Patients in remission had to be physically fit with no evidence of infection.

The CXR was required to show no active lesion. The ECG was performed to identify patients with significant cardiac ischaemia. No patient was rejected because of either an abnormal CXR or ECG.

The radionuclide ventriculogram is a non-invasive technique which has been reported to identify patients with anthracycline induced cardiotoxicity before clinical manifestations of cardiac failure develop (Alexander et al, 1979; Gottdiener et al, 1981)[1,81]. Later reports suggest that determinations during exercise may identify patients at risk more effectively (Dresdale et al, 1982; Druck et al, 1983)[56,57]. Radionuclide ventriculography was not available to us at the start of our study, and neither the patient (UPN B4) who developed left ven-

tricular failure on day -3 of the protocol, during the period of drug administration or the patient with lymphoma (UPN 61) who died in CCR 8 months post ABMT had had a radionuclide ventriculogram performed prior to ABMT. Only one patient who had a low resting left ventricular ejection fraction (LVEF) of 37% (normal LVEF >45%) had ABMT II delayed. The scan was repeated 5 months later when the LVEF had returned to 45%. The patient was found to have relapsed within a week of this scan and ABMT II was not therefore considered.

If a FBC demonstrated a thrombocytopenia of $<100x10^9/L$ even though the marrow appeared to be in remission, then the ABMT was delayed and the patient reassessed in one month, having received no further chemotherapy in the interval.

If the patient was anaemic but all other haematological parameters were acceptable then the harvest went ahead as planned and the patient was transfused.

No patient in the series had sufficiently abnormal renal function demonstrated on the biochemical screen to require a reduction in any of the drug doses or to defer the ABMT. One patient was found to have significantly deranged LFT's following induction therapy. This appears to have been due to nonA nonB post transfusion hepatitis.

The patient was deferred until her LFT's should either return to normal or stabilise when she might be reconsidered. She relapsed before ABMT I.

If an unexpected infection was discovered on microbiological screening eg. a urinary tract infection, then the infection was treated before proceeding. If a pathogenic bacteria was discovered eg Staph. aureus in the nose, then the patients harvest was not delayed but they were started on treatment with topical 'Naseptin'.

If screening the faeces revealed a potentially pathogenic organism, its sensitivity to gentamicin was recorded. In the event of gentamicin resistance the patient would be treated with amikacin as an alternative to gentamicin in the event of a pyrexia with no site of origin developing during the pancytopenic phase; see below.

No patient in this series was HBs antigen positive.

Relapsed Patients: The five patients treated as reinduction therapy for their acute leukaemia were the most seriously ill group. All were already pancytopenic and on parenteral antibiotics when they were treated with the chemotherapy of ABMT I. One patient (UPN 107) was known to have leukaemic infiltration of the kidneys.

LYMPHOMA

These patients were generally treated late in their disease, the above criteria were therefore modified and providing that the abnormalities discovered were consistent with the state of their disease they proceeded to ABMT as planned eg abnormal CXR, abnormal LFT's etc. One patient who was thought to have pyrexia relating to his disease was discovered to have a gram negative septicaemia. This was therefore treated prior to proceeding to ABMT.

During Admission For ABMT

Each patient was assessed daily by myself or another senior member of the team. A full blood count and a biochemical screen were performed at least on alternate days. Calcium was monitored once weekly and if noted to be low, a magnesium level was also obtained. A full microbiological screen was carried out once weekly with extra tests being performed as clinically indicated.

The haemoglobin level was maintained above 9 gm/dl by transfusion of donor red cells. Random platelet concentrates were transfused whenever the patients count fell below $20x10^9/L$ or there was evidence of bleeding.

Donor granulocytes were only considered if the patients granulocytes were $<0.2x10^9/L$ and they were severly ill, with an infection which was not responding to parenteral antibiotics.

Blood products were not irradiated prior to infusion post ABMT.

The biochemistry screen was used to assess the necessary electrolyte replacement. All patients on parenteral antibiotics required potassium supplements, some required calcium spplements and occasional patients also required magnesium supplements. The blood urea and creatinine allowed assessment of renal function and assisted in determining the dose of nephrotoxic antibiotics.

All significant positive microbiological isolates were treated according to their sensitivities.

Follow-up After Discharge

Patients were discharged when their neutrophils had risen above $0.5x10^9/L$ and their platelets were $>20x10^9/L$ unsupported. The neutrophil recovery generally lagged behind the platelet recovery to these levels for all patients recovering from ABMT I and for lymphoma patients

recovering from ABMT II (Table 1). The neutrophils of patients with acute leukaemia recovered more quickly than the platelets in most patients post ABMT II. Therefore, occasional patients who could attend easily on a daily basis for platelet transfusions have been discharged before their platelet count was sustained above $20x10^9/L$. After discharge patients were assessed twice weekly until the platelet count had returned to normal or until the patients count was stable with no bleeding manifestations, in those patients with delayed platelet recovery.

The UCH patients were followed up by myself or another member of the transplant team. Patients who had been referred from any distance were returned to the care of the referring haematologist, who sent details of their counts and progress to me for collection. Both the patients and their consultants were encouraged to phone and discuss any problems arising. Patients not returning to UCH for their regular follow-up are invited for review once a year.

I have reviewed all the temperature and drug charts, and all the entries in the notes of any patient who I did not personally supervise the care of.

Table 1. Comparison of the time to achieve platelet recovery of >$20x10^9$/L with the time at which neutrophils rose above $0.5x10^9$/L.

| | RISE IN PLATELETS COMPARED TO NEUTROPHILS: | | |
|---|---|---|---|
| | pre- or coincided | post- | death before recovery |
| AML ABMT I (n = 22) | 16 (76%) | 5 | 1 |
| ABMT II (n = 8) | 1 (12.5%) | 7 | |
| ALL ABMT I (n = 15) | 13 (87%) | 2 | |
| ABMT II (n = 9) | 3 (43%) | 4 | 2 |
| NHL ABMT I (n = 21) | 11 (69%) | 5 | 4 |
| ABMT II (n = 3) | 3 | | |
| HD ABMT I (n = 15) | 10 (83%) | 2 | 3 |
| ABMT II (n = 2) | 2 | | |
| TOTALS | 59 (70%) | 25 (30%) | |

Antibiotic Policy

Prophylactic antibiotics: Routine antifungal prophylaxis with oral nystatin or amphotericin was given.

Some patients also received antibacterial prophylaxis with cotrimoxazole, but this was abandoned in December 1983 because of increasing resistance of intestinal flora. No prophylactic antibacterial agents are given after discharge.

Antibiotics for treating episodes of pyrexia: Antibiotics were given for any infective episode and were started empirically whenever the temperature rose to >38.5$^{o}$C unless transfusion of blood products was in progress. In this instance, antibiotics were only started if the patient appeared ill or if the fever persisted at the end of the transfusion. High volume blood cultures (>15 mls) were taken at the inception of any fever and prior to instigating antibiotics.

If a focus of infection was identified then antibiotics appropriate to the likely infecting organism were initiated. If there was no obvious focus of infection then broad spectrum antibiotics were started at full dosage, as recommended for serious infections, after a repeat microbiological screen as outlined below.

Initially, the unit policy agreed with microbiological colleagues was to administer gentamicin and high dose benzyl penicillin parenterally, unless the patient was penicillin sensitive, when cefuroxime was substituted. If positive microbiology became available then the anti-

biotics were adjusted accordingly to any sensitivities reported. If there was no helpful microbiology, but the fever persisted after 48 hours, ceftazidime was substituted for the benzyl penicillin and metronidazole added. If fever still persisted, after a further 48 hours, then the addition of intravenous amphotericin was considered.

We later decided to enter patients in the current European Organisation for Research on Treatment of Cancer (EORTC)[59] trial of antibiotic therapy in neutropenic patients which meant patients received antibiotics according to the trial protocol (Figure 3).

## STATISTICAL METHODS

Statistical evaluation of results has been applied where appropriate. This has been either by a students t test, by the chi squared test or a Mantel test (Mantel N, 1966)[113].

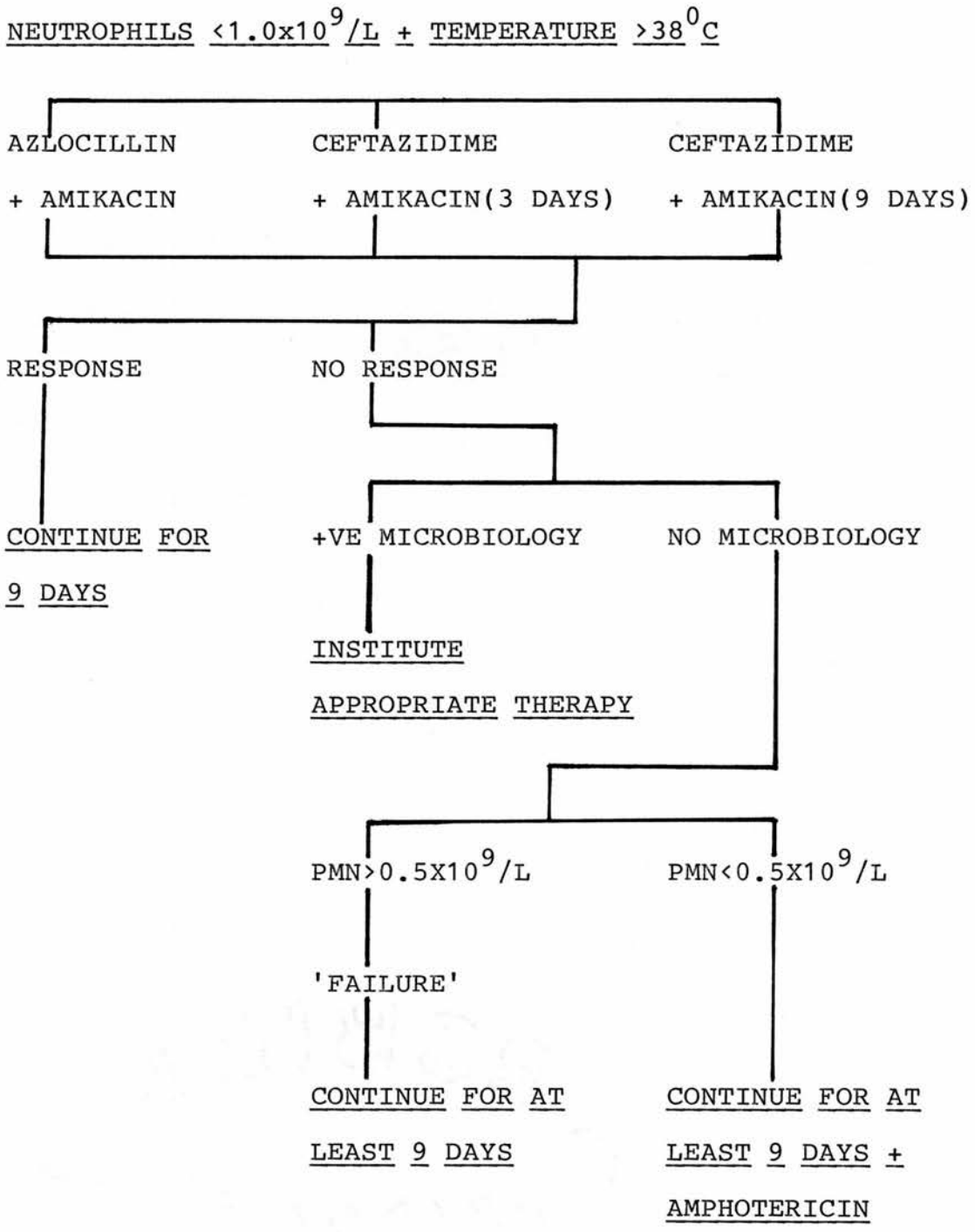



Figure 3. EORTC PROTOCOL.

# CHAPTER 3

## ACUTE MYELOID LEUKAEMIA

### INTRODUCTION

In 1957, Ronald Bodley Scott[158], the Queen's physician, wrote: "Acute leukaemia remains stubbornly fatal". Since then the application of, at first, single agents and then combination chemotherapy, has produced an ability to achieve a CR in most patients with acute leukaemia. However, in spite of this capability, most patients will relapse and ultimately die of their disease. Present approaches are therefore, designed to prolong DFS with the hope of possible cure.

If intensification of treatment for patients with AML in 1st CR, by using ABMT to allow high dose chemoradiotherapy, is to be successful, it must be demonstrated to be better than conventional chemotherapy without ABMT rescue, or if of similar efficacy, it must be demonstrated to have additional advantages eg shorter duration of chemotherapy.

If ABMT is to be used in preference to allografting then it needs to be shown to produce better long-term DFS. If results are similar, then ABMT may still be

preferred as a normal donor is not required.

## COMPARISON OF DIFFERENT THERAPEUTIC STRATEGIES

Comparison of the results of different treatment regimens in patients with AML is difficult because many of the reported regimens have excluded the older age groups which have the worst CR rates, shortest length of remission and survival (Keating et al, 1982; Beguin et al,1985)[100,14]. The exclusion of older patients also limits the value of any treatment as the majority of patients with AML present after 60 years of age. The median age of patients entered in the MRC AML8 trial was 53 years, but the median age of those notified to the trials office but not entered was 69 years (JKL Rees, personal communication). The CR rate in AML depends on the initial induction therapy and this has not been standardised although most remission induction regimens now employed include combinations of daunorubicin, cytosine arabinoside and thioguanine. They have been variously reported as achieving a 60-80% CR rate (Gale & Cline, 1977; Rees et al, 1977)[70,137]. The result of subsequent therapy is at least in part dependent on the induction regimen employed.

## PATIENT SELECTION

Patients who are treated with a BMT have usually been referred to a special centre from many other instituions and have not had uniform induction therapy nor do the transplant centres all use the same conditioning regimen. Patient selection has already occurred resulting in a better prognosis group because those who fail remission induction or who relapse quickly, do not usually get referred for BMT. Further selection of suitable transplant recipients occurs as only one in four siblings will be HLA identical, resulting in approximately 30-40% of patients with siblings having an HLA identical donor. Most centres do not consider patients above 40 years of age for allografts and it has even been suggested that patients should be <20 years of age (Foon & Gale, 1984)[67].

## CHEMOTHERAPY

In 1983, Weinstein et al[184], reported the updated results of the VAPA protocol, which is a 14 month intensive post induction chemotherapy protocol for use in both children and adults up to the age of 50 years. 107 patients were entered in the study and 70% of these achieved a CR. A Kaplan-Meier analysis of patients entering remission predicts that 56% of patients less than 18 years of age but only 45% of patients between 18

and 50 years of age will remain in CR at 3 years, (ie 31% of the original cohort).

Rees et al, 1985[138], published data from the Medical Research Council's AML 8 trial, suggesting that late intensification therapy was beneficial with a longer period of DFS and overall survival. The principal results of this trial have recently been published (Rees et al, 1986)[139]. A total of 1,127 patients were entered into this trial. Patients less than 13 years of age were originally excluded but then this restriction was lifted so there was no age restriction, median age was 49 years. CR rate varied depending upon age, but the overall CR rate was 67%. The overall median survival from diagnosis was just over 12 months, with a five year survival projected at 18% of the original cohort. As well as a beneficial effect from late intensification the study also demonstrated a small benefit to the use of 6 courses of consolidation rather than 2 but this did not achieve statistical significance. The impression that intensification of post induction treatment is beneficial argues in favour of more intensive regimens to improve long-term DFS.

This study also demonstrates a statistical benefit in relation to survival of the patients entered in the latter half of this trial although no criteria for admission eligibility or treatment were altered. This

seems likely to be due to improvement in support facilities, but demonstrates how the use of historical controls might give a false impression of advantage.

## BONE MARROW TRANSPLANTATION

Thomas ED, 1983[168], reported an overall DFS of 50% for patients with AML transplanted from an HLA identical donor following TBI and cylophosphamide whilst in first CR. If the patient population is divided by age then the long-term survival of those <20 years of age is 75% and and those >30 years of age 25% whilst those aged between 20 and 30 years of age have an intermediate survival. Deaths in the older age group being due to a much higher incidence of GVHD and pneumonitis with no increase in the relapse rate. The same group have also reported the results of a prospective comparison of BMT versus chemotherapy in 111 adult patients with AML, who were aged between 17-50 years. 81% acheived a CR. The patients were then divided into 2 groups dependent on whether or not they had a suitable donor. The chemotherapy and transplant group were reported to be similar with respect to age, white blood cell (WBC) count at diagnosis and FAB (French-American-British) subtype (Bennett et al, 1976)[15]. 17 of 33 (52%) of the BMT group are alive in CR 1.5-7 years post remission induction, whereas only 10 of the 43 chemotherapy patients (23%) are alive in remission

(Appelbaum & Thomas, 1985)[9].

The Royal Marsden (Powles et al, 1980)[131] reported a series of 50 patients, 22 treated by allogeneic BMT and 28 by chemotherapy. They found a significant reduction in leukaemic relapse after transplantation but survival at 3 years was not significantly improved (67% vs. 35% $p<0.1$). A subsequent update (Powles et al, 1982)[133] on 103 patients did report a survival advantage (56% vs. 24% $p<0.005$). The same difficulty, in relation to patient selection, applied to the Marsden study as well as the Seattle study, but the patients who received BMT in this study had received their remission induction therapy at other centres, whereas all the patients treated with chemotherapy were induced at the Marsden.

Autografting does not have the severe age restriction of allografting and an HLA identical sibling is not required. Patient selection will still occur however, at the referring institution or by early relapse of disease. A further exclusion in either autologous or allogeneic transplantation is patients who refuse this treatment option.

## CHOICE OF CONDITIONING REGIMEN FOR ABMT

The same pre-graft conditioning as for allogeneic

transplants could be used for ABMT, but the relapse rate after a syngeneic graft is high suggesting failure to eradicate host disease (Fefer et al, 1981)[62]. After ABMT the relapse rate might be expected to be higher than after a syngeneic graft in view of the theoretical possibility of reinfusing residual disease with the autologous marrow.

There are therefore, two important considerations in the choice of a protocol for conditioning the patient pre-ABMT, the eradication of disease in the patient and the eradication of residual disease in the harvested marrow.

When we first developed our cryopreservation technique we ran a small pilot protocol in which bone marrow was harvested during first remission (CR1) from patients with acute leukaemia and upon relapse they were to be treated with 10 gray TBI and 60 mg/kg cyclophosphamide given on two consecutive days prior to the TBI, as used in allografts by the Seattle group. The stored autologous marrow from first remission was to be used to rescue the patient from the aplasia thus produced. The plan was to use this as their reinduction therapy. The allogeneic data from Thomas et al, 1977[172] did not lead us to expect a prolonged remission without further therapy, but we were concerned that further treatment immediately post autograft might result in prolonged cytopenias. We

therefore postponed the possibility of further consolidation or maintenance therapy.

Four patients were treated, 2 had relapsed AML and 2 relapsed ALL. One patient received only 8 gray TBI with the cyclophosphamide and failed to attain a remission. One patient appeared to be free of disease as assessed by a bone marrow aspirate at day 28, but remained hypoplastic until relapse at 44 days post ABMT. The other 2 patients achieved a complete remission with full haematological recovery, but relapsed again at 5 and 6 months post ABMT. One of these patients had a second remission lasting more than twice the period of time between harvest of the marrow and relapse, suggesting some reduction of the residual disease in the autologous marrow from the procedure of harvesting, cryopreservation and reinfusion alone, without any other purging manouvre.

Following this experience and in the light of early reports in the literature (Dicke et al, 1979; Kaizer et al, 1981)[53,97] we decided on a double autograft technique. We felt this had several advantages:

Eradication of residual leukaemia in the host: If a single dose of massive chemoradiotherapy may eradicate disease in some but not all patients, then to repeat the procedure should produce a greater tumour kill. TBI is an unsuitable modality for a double protocol. It has

occasionally been used at a much lower dose a second time in patients who have relapsed post allogeneic graft (P Stewart, personal communication), but its efficacy in this situation is doubtful, and the toxicity, particularly from interstitial pneumonitis, would be expected to be high. We decided on a combination chemotherapy protocol using the same drug regimen for the first and second ABMT.

Graw et al, 1974[82], reported the successful use of BACT chemotherapy (Table 2) to condition patients with acute leukaemia prior to allogeneic bone marrow transplantation. They also used the regimen in two patients prior to autologous bone marrow transplantation, both of whom died of sepsis, one at day 14 before any evidence of engraftment and one at day 28 when the bone marrow was hypocellular with 20% blasts. In 1978, Appelbaum et al[5], reported the successful use of BACT chemotherapy (Table 2) followed by ABMT in patients with relapsed non-Hodgkin's lymphoma. They demonstrated a definite reduction in the time to haematological recovery for patients who received autologous marrow post treatment with BACT chemotherapy when compared with controls who received no marrow.

Table 2. BACT chemotherapy regimen (Graw et al, 1974)[82].

| DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE 45 MG / KG | * | * | * | * | | | |
| BCNU 200 MG / $M^2$ | * | | | | | | |
| CYTOSINE ARABINOSIDE 100 MG / $M^2$ | ** | ** | ** | * | | | |
| THIOGUANINE 100 MG / $M^2$ | ** | ** | ** | * | | | |
| ABMT | | | | | | * | |

BACT chemotherapy regimen (Appelbaum et al, 1978)[5].

| DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE 45 MG / KG | | * | * | * | * | | |
| BCNU 200 MG / $M^2$ | * | | | | | | |
| CYTOSINE ARABINOSIDE 100 MG / $M^2$ | | ** | ** | ** | ** | | |
| THIOGUANINE 100 MG / $M^2$ | | ** | ** | ** | ** | | |
| ABMT | | | | | | | * |

Gorin et al, 1979[78], used a modified BACT regimen - TACC in which the BCNU was replaced by CCNU (Table 3), followed by ABMT in 8 of 12 patients. 4 patients had solid tumours and 8 acute leukaemia. They concluded that the autologous marrow was beneficial and would reduce the period of aplasia by approximately 50%, but that TACC high dose combination chemotherapy did not produce irreversible aplasia or eradicate the leukaemia.

Table 3. TACC chemotherapy regimen.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE 45 MG / KG | * | * | * | * | | | |
| CCNU 200 MG / $M^2$ | | * | | | | | |
| CYTOSINE ARABINOSIDE 100 MG / $M^2$ | ** | ** | ** | ** | | | |
| THIOGUANINE 100 MG / $M^2$ | ** | ** | ** | ** | | | |
| ABMT | | | | | | * | |

We decided to adopt our own variation of the BACT protocol as the basis of our chemotherapy regimen. The dose of drugs used in both BACT and TACC had not produced marrow ablation as judged by the successful haemato-

logical recovery of patients who did not receive any marrow rescue. We therefore decided to increase the dose of BCNU to 300 $mg/m^2$. We also felt the addition of an anthracycline was important in the treatment of patients with AML and as we assumed all patients would already have received daunorubicin in their induction regimes we chose to use adriamycin. High dose cyclophosphamide used in combination chemotherapy, has been reported as producing cardiotoxicity (Zeigler et al, 1976)[191], as we did not wish to induce unacceptable cardiotoxicity by adding adriamycin in a high dose we decided to add it at a conventional dose of 50 $mg/m^2$. The same combination chemotherapy protocol being used for ABMT I & II (Table 4).

The use of a second ABMT also removed the worry of producing prolonged cytopenia if conventional chemotherapy was to be used immediately post ABMT.

Eradication of residual leukaemia in the marrow: We argued that a double protocol would effect a form of 'in vivo' purging. For example if the marrow at the time of the first harvest contained X tumour cells then post harvest the cryopreserved marrow would contain only 2% X assuming a harvest of 2% of the total marrow content (Faille et al, 1981)[60] and no differential loss of disease and normal stem cells during cryopreservation. If leukaemic and normal marrow cells have the same regrowth

potential then they will remain in the same proportions post ABMT. However, the success of induction regimes which render the patients marrow severely hypoplastic relies on normal haemopoietic tissue having a regenerative advantage to the leukaemic population. After a second ABMT therefore, the residual population of leukaemic cells should be considerably less than after a single ABMT. This number might fall below the critical level at which the body's own defences might be able to eliminate or contain any residual disease, total elimination being perhaps unnecessary.

Table 4. UCH double chemotherapy regimen.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE | * | * | * | | | | |
| 1.5 G / $M^2$ | | | | | | | |
| BCNU | * | | | | | | |
| 300 MG / $M^2$ | | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | |
| THIOGUANINE | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | |
| ADRIAMYCIN | * | | | | | | |
| 50 MG / $M^2$ | | | | | | | |
| ABMT | | | | | | * | |

PATIENTS

24 adult patients with AML have been treated between January 1981 and January 1985. The median age was 40 years (range 19-57 years). 16 patients were autografted in first remission, 5 in second remission and 3 patients who had marrow harvested during first remission were reinduced with the regimen at relapse. Further details are given in Table 5.

BONE MARROW HARVESTING, CRYOPRESERVATION AND REINFUSION

Bone marrow was harvested, cryopreserved and reinfused as previously described (Chapter 2; Linch et al, 1982)[107]. 19 patients were harvested in CR1 and 5 in second remission (CR2). The mean number of nucleated cells frozen was $1.9 \times 10^8$ cells/kg body weight (range $0.6-3.1 \times 10^8$ cells/kg). The time for which the marrow was stored in liquid nitrogen before both ABMT I and II, is shown in Table 6.

TREATMENT PLAN

This is outlined in Figure 4. The first bone marrow harvest was performed where possible, following recovery from consolidation therapy in first remission patients and as soon as possible following reinduction therapy in the 5 patients treated in second remission.

TABLE 5. PATIENT CHARACTERISTICS: AML

PATIENTS TREATED WITH ABMT DURING IST REMISSION

| UPN | Sex | Age | FAB CLASS. | NO. OF GRAFTS | DIAG ->CR | CR-> ABMT | DIAG-> ABMT | STATUS POST ABMT | DFS SURV. POST ABMT | TOTAL SURV. | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | M | 25 | M1 | 2 | 2 | 2 | 4 | CR | 61+ | 65+ | A & W |
| 30 | M | 38 | M3 | 1 | 1 | 7 | 8 | CR | 55+ | 63+ | A & W |
| 105 | F | 43 | M4 | 2 | 2 | 5 | 8 | CR | 31+ | 39+ | A & W |
| 108 | F | 39 | M1 | 2 | 2 | 7 | 9 | CR | 30+ | 39+ | A & W |
| 128 | F | 32 | M2 | 1 | 1 | 5 | 6 | CR | 25+ | 31+ | A & W |
| 131 | F | 45 | M4 | 1 | 3 | 5 | 8 | CR | 24+ | 32+ | A & W |
| 132 | M | 47 | M1 | 1 | 2 | 4 | 6 | CR | 11 | 25 | DEAD |
| B3 | M | 42 | M4 | 1 | 3 | 1 | 4 | CR | 2 | 7 | DEAD |
| B4 | F | 55 | M2 | 1 | 3 | 10 | 13 | CR | 6 | 21 | DEAD |
| 143 | M | 49 | M1 | 2 | 1 | 3 | 4 | CR | 20+ | 24+ | A & W |
| 147 | M | 35 | M5 | 2 | 2 | 4 | 6 | CR | 19+ | 25+ | A & W |
| 148 | M | 26 | M1 | 2 | 1 | 6 | 7 | CR | 19+ | 26+ | A & W |
| 156 | F | 19 | M2 | 1 | 3 | 9 | 12 | CR | 15 | 29 | DEAD |
| 160 | M | 36 | M1 | 1 | 2 | 7 | 9 | CR | 16+ | 25+ | A & W |
| 163 | F | 36 | M4 | 1 | 4 | 2 | 6 | CR | 7 | 13 | DEAD |
| 174 | F | 40 | M2 | 1 | 3 | 4 | 7 | REL *** | 0 | 13 | DEAD |

PATIENTS TREATED WITH ABMT AS REINDUCTION THERAPY OR IN 2ND REMISSION

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 41*/** | F | 57 | M2 | 1 | 2 | 20 | 22 | CR | 7 | 32 | DEAD |
| 55 | F | 31 | M1 | 1 | 2 | 5 | 7 | CR | 2 | 15 | DEAD |
| 92*/** | M | 49 | M1 | 1 | 3 | 22 | 25 | NE Died day 12 | | 25 | DEAD |
| 98 | M | 44 | M1 | 2 | 6 | 4 | 10 | CR | 8 | 19 | DEAD |
| 100*/** | M | 51 | M5 | 1 | 2 | 6 | 8 | CR | 3 | 11 | DEAD |
| 122 | F | 34 | M5 | 1 | 1 | 6 | 7 | CR | 2 | 14 | DEAD |
| 125* | M | 21 | M1 | 2 | 2 | 35 | 37 | CR | 5 | 43 | DEAD |
| 129 | M | 51 | M6 | 1 | 1 | 35 | 36 | CR | 13 | 50 | DEAD |

UPN = Unique Patient Number. All patients grafted in the Bloomsbury Transplant Unit have been given consecutive numbers dependent only on the date of ABMT. Where the UPN has been prefixed with a 'B' the patients were grafted at the Queen Elizabeth Hospital, Birmingham; FAB CLASS. = French, American, British classification; NO. = Number; DIAG = Diagnosis; CR = Complete remission; DFS SURV. = Disease free survival; NE = Not Evaluable.

* Patients who were harvested in 1st remission.

** Patients who were treated in 1st relapse.

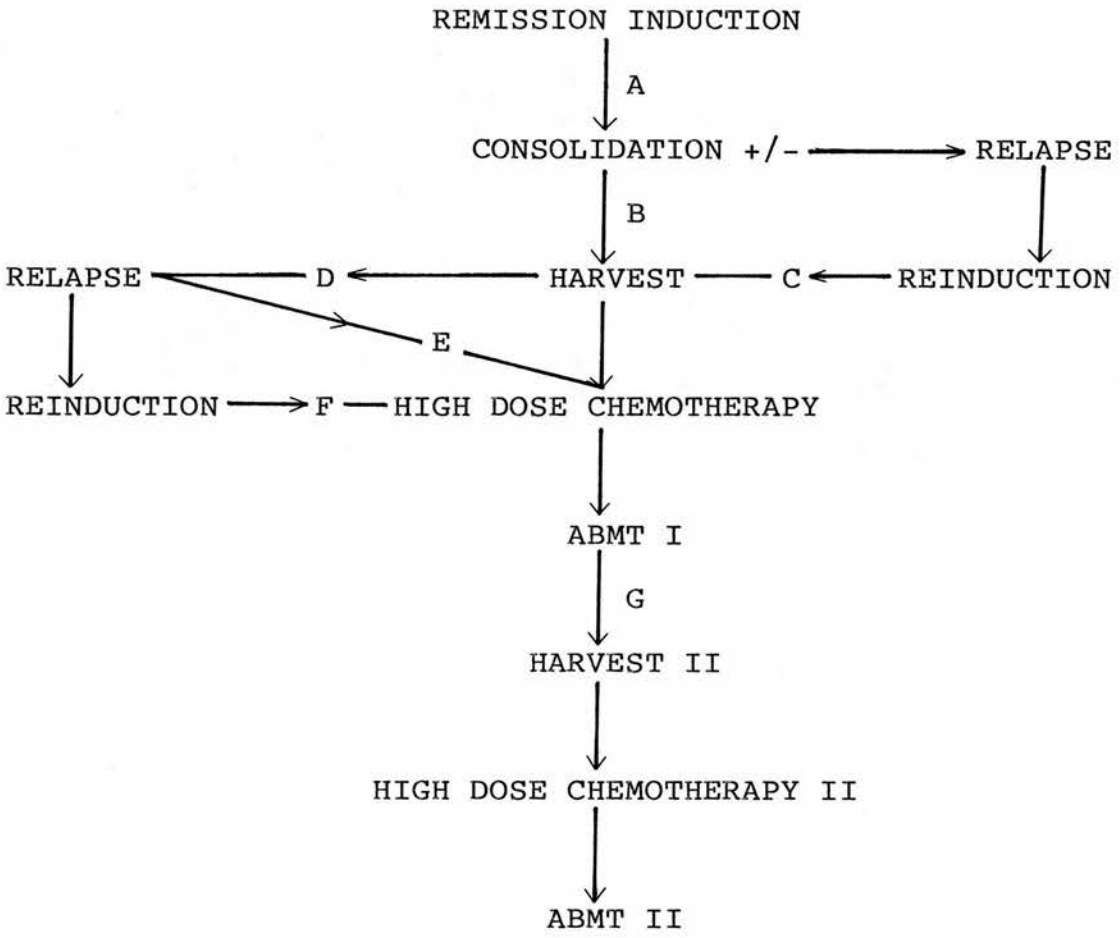
*** Although performed in apparent remission this patient regenerated with disease.

All time intervals are recorded as months: + indicates continuing survival.

Table 6. Time for which the marrow was stored in days:AML

| | ABMT I | | | ABMT II | | |
|---|---|---|---|---|---|---|
| | Mean | Range | Pat Nos | Mean | Range | Pat Nos |
| CR1 | 26 ( Median 10 ) | 7-140 | n = 16 | 11 | 8-16 | n = 6 |
| CR2 | 11 | 5-24 | n = 5 | 10 | 8-12 | n = 2 |
| HARVEST IN CR1 TREATED AFTER RELAPSE | 158 | 22*-252 | n = 3 | | | |

* This patient was originally harvested when thought to be in CR1. On review of his pre-harvest marrow, it was clear he was in early relapse. As he had already had a lot of treatment it was decided to proceed to ABMT with the minimally involved marrow already harvested. He remained in good health post ABMT for 3 months without further treatment. He has been included in the group of patients treated at first relapse.




A All patients

B 20 patients harvested in 1st remission

C 4 patients harvested in 2nd remission

D 4 patients harvested in 1st remission but not treated

E 3 patients treated in relapse

F 1 patient reinduced before treatment

G 8 patients who had ABMT II

See text for details of treatment regimens.

Figure 4. Treatment plan : AML

All first remission patients were treated within 13 months of their diagnosis, mean 8 months (range 4-13 months).

8 patients have completed a second autograft. All had their marrow reharvested as soon as possible after full haematological recovery and proceeded directly to ABMT II. The reasons for not proceeding to ABMT II are shown in Table 7.

Table 7. Reasons for not proceeding to ABMT II: AML

| | AML |
|---|---|
| DEATH IN PART I | 1 |
| RELAPSE | 4 (1 CNS) |
| DELAYED HAEM. RECOVERY | 5 |
| REFUSED | 4 |
| OTHER * | 2 |
| TOTALS | 16 |

* 1 Patient who had a reduced resting left ventricular ejection fraction on radionuclide ventriculogram.
1 Patient who had very slow physical recovery post ABMT I.

RESULTS

Response to therapy.

First remission AML: 16 patients have so far been treated. Ten patients (62.5%) continue in unmaintained remission 62, 55, 32, 28, 25, 24, 20, 19, 19 and 15 months post ABMT, with no procedural deaths. Six have relapsed 1, 2, 6, 7, 11 and 15 months post ABMT (Figure 5).

Relapsed AML: Three patients with AML were treated with this regime as reinduction therapy following relapse. Two achieved a complete remission, one patient (UPN 92) died during aplasia of an intra-cerebral haemorrhage. The two surviving patients did not go on to receive ABMT II because of delayed haematological recovery. Both have relapsed and died, relapse occurring 3 and 7 months post ABMT (Figure 5).

Second Remission AML: Five patients were treated in second remission, two received both ABMT I & II, all have died in relapse, 6, 7, 8, 9 and 14 months post ABMT (Figure 5).

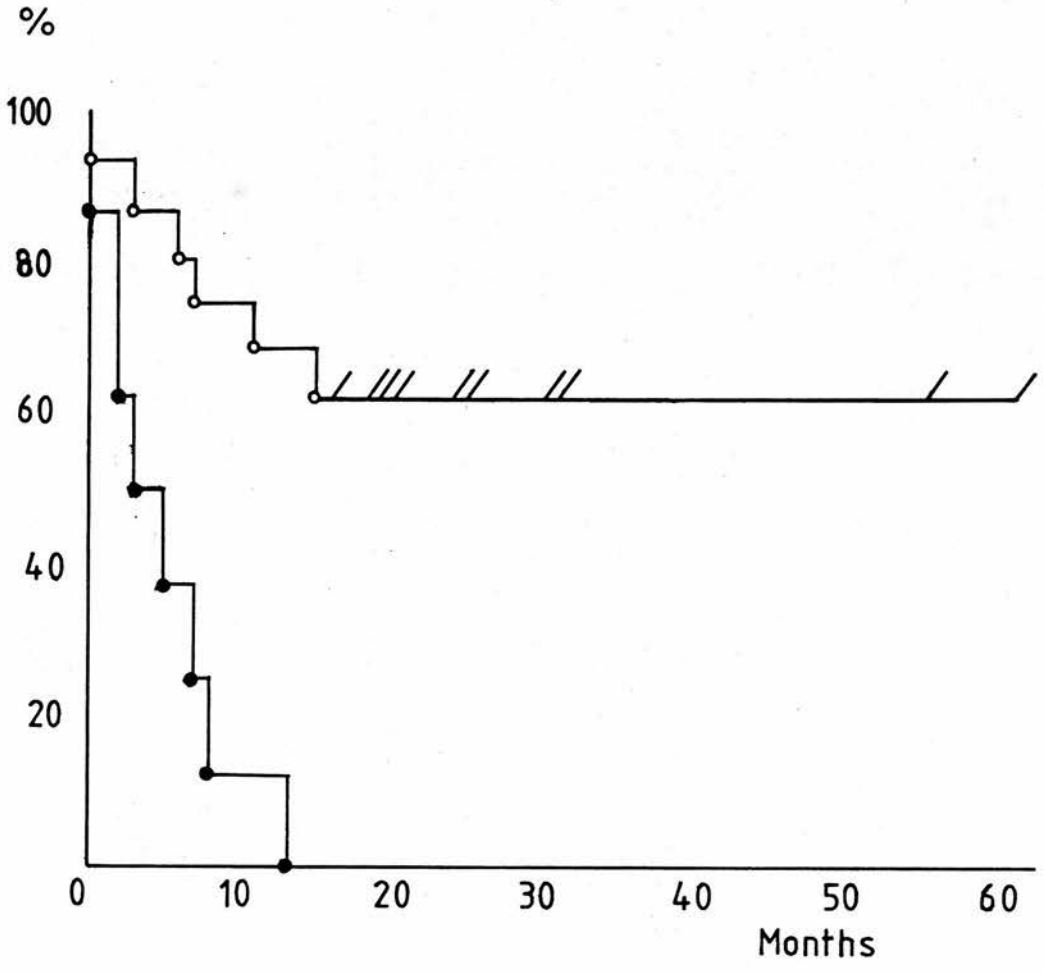



Figure 5. DFS in patients with AML.

Patients treated in CR1 (n=16) o—o

Patients treated in CR2 or relapse (n=8) •—•

DISCUSSION

An increasing number of high dose chemotherapy regimens utilising autologous bone marrow transplant to alleviate the severe haematological toxicity, are being used for treating patients with acute leukaemia, lymphoma and other solid tumours, in an attempt to prolong disease free survival by allowing increases in the tumoricidal doses of chemotherapy. In acute leukaemia, this technique suffers from the disadvantage that residual leukaemic cells are likely to be reinfused with the autologous marrow. The autologous marrow has been used unpurged (Gorin et al, 1985; Burnett et al, 1984)[79,30] or has been purged 'in vitro' in an attempt to remove presumed residual disease (Ritz & Schlossman, 1982; Laporte et al, 1984)[142,104], although the need for purging has not yet been proven.

There is no convincing evidence of benefit from purging the autologous marrow in any situation (Gorin et al, 1985)[79] and for AML in particular there is no evidence of altered sensitivity of leukaemic cells from normal progenitor cells when treated with cytotoxic drugs 'in vitro' (Douay et al, 1984)[55] nor is there a suitable monoclonal antibody available which can distinguish between these cell types. We do not use 'in vitro' purging but feel that repeating the procedure a second time should reduce the leukaemic burden further and

effect 'in vivo' purging.

Ten (62.5%) of our patients with AML treated with ABMT as early intensification therapy in first remission continue in unmaintained remission with a minimum follow up time of 16 months, median 24 months, range 16-61 months (Figure 5). Our figures for first remission AML in adults are highly encouraging compared to the results of more conventional chemotherapy (Weinstein et al, 1983; Rees et al, 1985; Wolff et al, 1985)[184,138,187] and allogeneic BMT where the mortality rate in patients over 30 years of age is high (70-75%) with most deaths being due to GVHD or interstitial pneumonitis (Thomas ED, 1983)[168]. Thirteen of our patients are over 30 years of age and their survival is still 62%, with a minimum follow up of 16 months.

Massive chemotherapy with ABMT rescue appears effective at inducing a CR in relapsed patients with AML (two of three patients with one death occurring during aplasia). Five of our patients were treated in second remission. These seven patients have relapsed again within 13 months (2, 2, 3, 5, 7, 8 and 13 months) and have died (Figure 5).

It has been suggested that patients undergoing either allogeneic BMT or ABMT are a selected population with a better prognosis, as pre-BMT delays tend to occur for many reasons, thus the major threat of relapse has passed. Burnett et al, 1986[31], have reported improved results following ABMT, when the procedure is delayed until at least 4 months after CR1 is obtained.

In our own series of 16 patients with AML, where the intention was to progress to ABMT as early as possible following induction of CR1 and one course of consolidation therapy, 5 patients were treated with ABMT within 4 months of induction of CR1, 9 patients between 4-8 months and only 2 were treated after more than 8 months. Although the group transplanted early in CR1 fared worse than the 4-8 month group the 2 patients receiving ABMT as late consolidation beyond one year have both relapsed and died (Figure 6).

If BMT, either allografting or autografting is to be beneficial, then the earlier it is applied to try and prevent relapse in patients destined to relapse early, the better overall survival of patients with AML is likely to be.

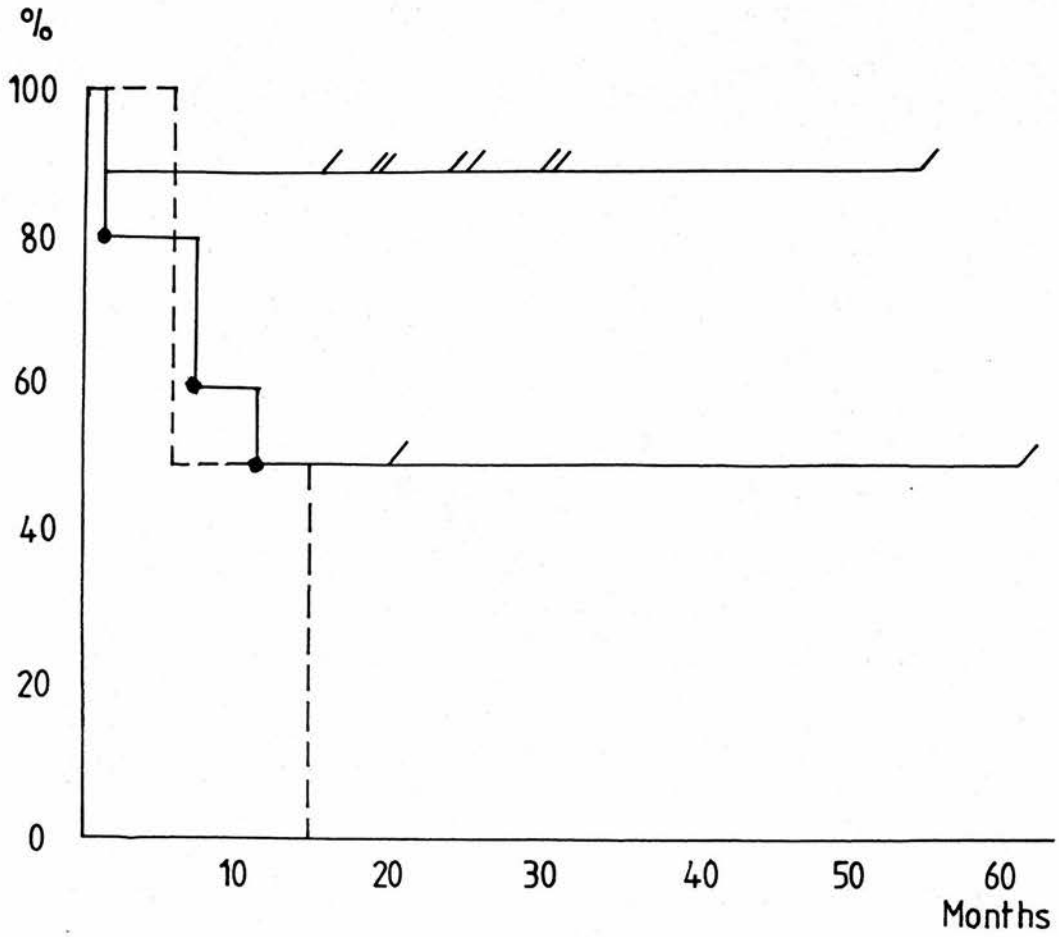



Figure 6. DFS post ABMT:

Patients treated <4/12 (n=5)

4-8/12 (n=9)

>8/12 (n=2)

after achieving CR1.

The need for a double autograft is unproven. Maraninchi et al, 1984[114], have also advocated a double protocol. Four of their long-term survivors had ABMT I and II (11+, 11+, 28+, 29+) and of ten relapses eight patients received only ABMT I.

In our patients with AML, the six patients who received a double autograft as consolidation therapy in first remission remain well in unmaintained CR, between 19 and 61 months post ABMT. Ten patients had only ABMT I and six have already relapsed between 1-15 months post ABMT, median 6 months (Figure 7).

The four remaining patients in first unmaintained remission are now 16, 24, 25 and 55 months post ABMT. The relapse of six (60%) of patients with AML treated in first CR who did not have ABMT II whilst there are no relapses in the six patients who had ABMT I & II encourages us to believe that the second ABMT has resulted in a greater reduction of host disease, with the possibility of cure. It could also mean that delay in haematological recovery after ABMT I which is the main reason for failing to proceed to ABMT II may be a characteristic of more aggressive or resistant disease and such patients may be a poor prognosis group, irrespective of whether they receive ABMT II or not.

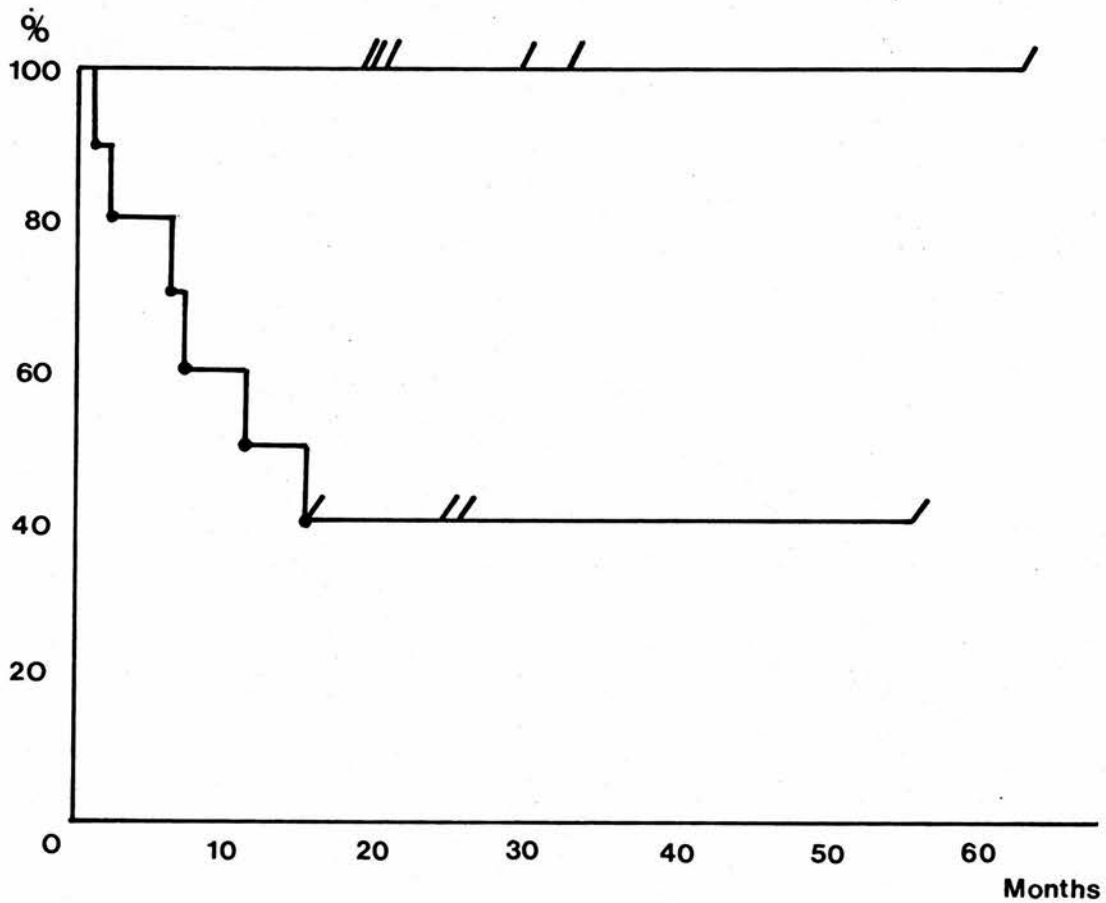



Figure 7. DFS in AML in CR1: ABMT I vs ABMT I & II.

ABMT I (n=10)

ABMT I & II (n=6)

The collective EBMTG data (Gorin et al, 1985)[79], which includes our group of patients, showed a trend in favour of double autografting when compared to single autografts for DFS: 79% versus 48% at 640 days, ($p<0.1$). Numbers are small and the differences do not achieve statistical significance. If encouraging results are maintained it will not be possible to determine if this is due to improved leukaemic eradication or 'in vivo' purging. This will depend on the development of sensitive assays for minimal residual disease.

The best prognostic determinant in our series of patients with AML treated in CR1 is the length of time from diagnosis to achieve CR1 (Table 8). This appears a better discriminator than whether or not the patient receives both ABMT I and II ($p<0.01$ vs $p<0.05$).

Table 8. The time taken to achieve CR1 as a prognostic indicator in patients with AML treated in CR1

| UPN | TIME FROM DIAG TO CR IN DAYS | CURRENT STATUS | NO OF GRAFTS |
|---|---|---|---|
| Patients who took >2/12 | | | |
| B3 | 132 | REL | 1 |
| 163 | 123 | REL | 1 |
| 174 | 108 | REL | 1 |
| 131 | 97 | CR | 1 |
| 156 | 90 | REL | 1 |
| 105 | 74 | CR | 2 |
| 132 | 72 | REL | 1 |
| B4 | 71 | REL | 1 |
| Patients who took <2/12 | | | |
| 160 | 60 | CR | 1 |
| 19 | 55 | CR | 2 |
| 147 | 54 | CR | 2 |
| 108 | 43 | CR | 2 |
| 148 | 39 | CR | 2 |
| 128 | 35 | CR | 1 |
| 30 | 33 | CR | 1 |
| 143 | 20 | CR | 2 |
| Minimum follow-up is 16 months | | | |

UPN: Unique Patient Number

Diag: Diagnosis

No: Number

No patient who achieved a CR in less than 2 months (8 patients) has relapsed, whether or not they had ABMT I or ABMT I & II, whereas 6 of the 8 patients who took more than 2 months to achieve their 1st CR have already relapsed (Figure 8). 5 of the 6 patients who had ABMT I & II are in the group of patients who remitted quickly, this is likely to be explained by less pre-ABMT chemotherapy resulting in better marrow yields and faster haematological recovery, such that patients were able to tolerate two procedures better than extensively treated patients. Patients who enter CR easily are likely to have more sensitive disease and it may even be that a second autograft is not required in this group.

It may become possible as further numbers of patients are treated with this protocol to determine whether or not a second ABMT is improving survival in either the early or late responders or perhaps in both.

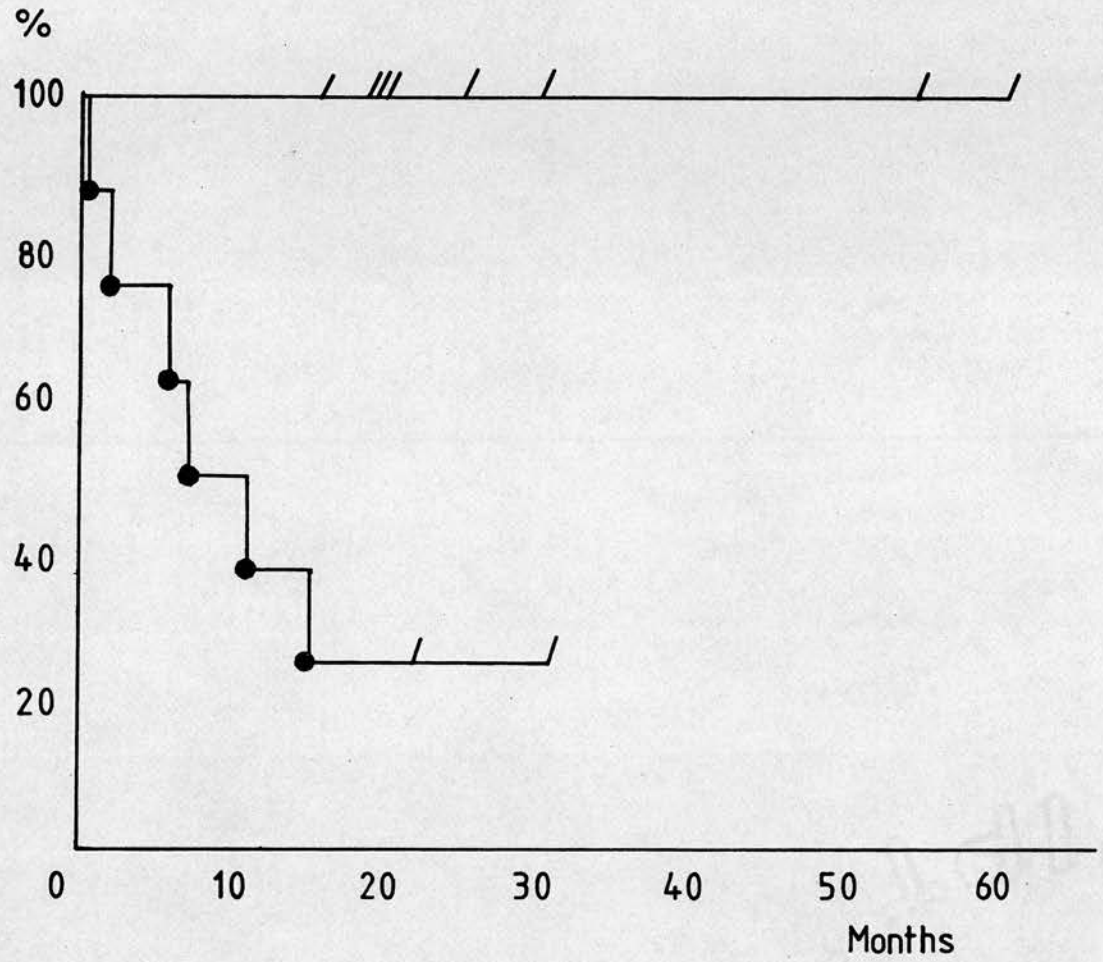



Figure 8. DFS in AML in CR1:

Patients who achieved CR1 in <2/12 (n=8)

Patients who took >2/12 (n=8)

The optimum time to proceed to ABMT has yet to be determined as well as what the best conditioning regimen might be and whether a double protocol is necessary. The use of the high dose chemotherapy regime employed here with ABMT rescue appears to be a useful approach to intensify consolidation treatment of the adult patient with AML in first remission and perhaps should already be considered as the most appropriate therapy for patients over 30 years of age whether or not they have a suitable allogeneic donor.

There is little clear benefit from this particular intensive regime for patients with AML treated after first remission.

Yeager et al, 1986[189], have reported the use of ABMT following conditioning with Busulphan/Cyclophosphamide in relapsed patients. The autologous remission marrow was incubated with 4 hydroperoxycyclophosphamide (4HC) before cryopreservation and reinfusion. DFS for CR2 and CR3 patients is 50%, median duration 17 months.

The use of the time to acheive CR1 as a prognostic indicator post ABMT needs to be confirmed in a larger series of patients. If it remains significant it will be valuable in comparing the different prognostic groups when treated with different conditioning regimens and may ultimately be able to predict which patients with AML

when treated in first CR will do well without needing a second autograft.

# CHAPTER 4

## ACUTE LYMPHOBLASTIC LEUKAEMIA

### INTRODUCTION

The use of ABMT in patients with ALL to be justified, must, as in patients with AML, be shown to produce better DFS than either chemotherapy regimens without ABMT or allogeneic BMT. However, survival following treatment for ALL is quite different to that of patients treated for AML. The two most striking differences are the success of induction consolidation maintenance chemotherapy regimens in achieving a cure rate in children of >50% and the high relapse rate post allogeneic transplant which limits its success (Sanders et al, 1985)[150].

### CHILDHOOD ALL

Therapeutic results in childhood acute lymphoblastic leukaemia have improved progressively with CR rates of over 90% and 5 year disease free survival in more than 40-50% (Sallan et al, 1978; Haghbin et al, 1980; Riehm et al, 1980)[149,84,141].

Children with ALL are now able to be divided into good

and poor prognosis groups at presentation. The most important prognostic indicator being the peripheral blast cell count and the patients age and sex (Chessels JM, 1982)[41].

Children, particularly girls, with a low peripheral blast cell count at presentation, represent a group with a good prognosis who should do well on conventional chemotherapy regimes without ABMT.

Relapse

Once a patient has relapsed during initial therapy, although a further CR may be achieved median duration of remisson is only short eg. 13 weeks (Chessels & Cornbleet, 1979)[42]. The Childrens Cancer Study group (Baum et al, 1983)[13] have reported one of the most successful regimens to date in maintaining a second or subsequent remission using a modified Capizzi regimen (Capizzi et al, 1974)[36] which gives a predicted median duration of remission of 57 weeks with 10 patients (33%) remaining in CR at 1 year and 3 (10%) at 2 years. The Paediatric Oncology Group Study (Rivera et al, 1986)[144] reports the results of an intensive reinduction and continuation chemotherapy protocol, for children with first bone marrow relapse of ALL, occurring whist still on treatment or within 6/12 of cessation of treatment.

They achieved an 80% induction of CR2. The best predictor for the length of CR2 was the time for which the patient had been in CR1. No patient who had an initial CR of <18/12 remains in CR2 at 30 months, whereas more than 50% of patients who had an initial CR of >18/12 remain in CR2 for more than 36 months. Patients who relapse after treatment is stopped may have a second prolonged CR with chemotherapy but not all results agree (Mauer AM, 1980; Sallan & Hitchcock-Bryan, 1981)[117,148].

Long-term remission is now the rule in most children and so they would not normally be considered for bone marrow transplantation (BMT) in first CR. After relapse has occurred, although a further long remission may be possible the patient will ultimately relapse again and die of their disease (Johnson et al, 1981)[95]. Children should therefore be considered for BMT during second CR.

ADULT ALL

In adults the results of remission induction therapy are not as good as reported in children, with recent multicentre trials reporting CR rates of 61-85% with remission duration of 9-25 months (Lister et al, 1978; Amadori et al, 1980; Omura et al, 1980)[110,2,123].

In a recent review of therapy for adults with ALL,

Jacobs & Gale, 1984[93], report the results of several trials of induction continuation therapy with CR rates of 72-92% and a median duration of survival of 62 months on the L10 protocol (Schauer et al, 1983)[156]. The L10 protocol is a multi-drug induction regimen employing vincristine, prednisolone and adriamycin, followed by an intensive consolidation and maintenance chemotherapy programme. These encouraging results are much more similar to the results in children.

Prognostic indicators

The factors affecting prognosis in adults are similar to children; sex has only a small influence on the outcome but of increasing importance is cytogenetic analysis (Bloomfield et al, 1986)[19].

In a German multicentre study (Hoelzer et al, 1984)[89], they initially treated all adult patients with the same regimen and from this study they identified various prognostic indicators which were able to predict a high likelihood of relapse. Having now identified this group, they treat patients with these characteristics with a different more aggressive induction regimen. The most recent analysis suggests that these patients now do as well as the patients identified as having a good prognosis at presentation (Hoelzer et al, 1986)[91]. T cell

patients although small in number seem to have a particularly good prognosis on this regimen (Hoelzer et al, 1985)[90].

Relapse

Once relapse has occurred the chance of long-term survival is poor.

In a prospective study (Johnson et al, 1981)[95] patients with ALL in 2nd or subsequent CR were given BMT if a matched sibling donor was available or treated with chemotherapy in the absence of a suitable donor. Of 21 patients treated with chemotherapy all have relapsed and 1 remains alive, while 8 of 24 BMT recipients continue in unmaintained CR with a follow-up of 3-6 years.

ALLOGENEIC BMT

The position of allografting for patients with ALL is not clear. Following BMT for ALL the complication rate is the same as after BMT for AML but there is a much higher relapse rate. The leukaemic relapse rate is more than 50% after allografting for ALL in 2nd or subsequent CR (Sanders et al, 1985)[150] but still seems to offer the best hope of long-term survival and cure after a patient

with ALL has relapsed (Thomas et al, 1983)[175]. By analogy with the improvement in survival in patients with AML when allografted in 1st CR rather than at relapse or a later remission, ALL patients considered to have a poor prognosis have been allografted whilst in 1st CR but numbers are still small. Data from the European Group for Bone Marrow Transplantation (EGBMT)(Zwaan et al, 1986)[192] suggests that relapse rates are less than 50% for patients with ALL transplanted in 1st CR.

Since the majority of recurrent leukaemias are of the original host type (Boyd et al,1982)[23] current efforts are being directed at eradicating the leukaemic clone. At Sloane Kettering (Dinsmore et al, 1983)[54] they are using 'hyper-fractionated' irradiation with only a 14% relapse rate for patients transplanted in 2nd CR. Others are giving additional chemotherapy post BMT (Woods et al, 1983)[188], in Seattle there is a trial of interferon (Thomas ED, 1983)[168], and yet others are trying alternative conditioning regimens (Santos et al, 1986)[155].

The relapse rate is so high in patients post-allogeneic transplantation for ALL, that conditioning regimens will need to be stronger pre-ABMT. It is unlikely there will be a GVL effect and leukaemic cells may still reside in the autologous remission marrow. The depletion of these leukaemic cells by physical (Dicke et

al, 1979)[53], immunological (Ritz & Schlossman, 1982)[142], and pharmacological techniques ( Kaizer et al, 1981)[97] offer promise for the future. The EBMTG results have so far failed to demonstrate any benefit from purging (Gorin & Aegerter, 1986)[80].

Autologous BMT

Adult patients with ALL have a much worse prognosis than children and therefore, it is these patients with ALL who are being included in trials of high dose chemotherapy regimens during CR1. All patients following relapse have a poor prognosis and represent the bulk of patients receiving this form of treatment at the present time.

PATIENTS

18 patients with acute lymphoblastic leukaemia have been treated between November 1981 and November 1984. The median age was 22 years (range 6-49 years). 8 adult patients were autografted in first remission, 7 others (5 adults and two children aged 6 and 13 years) were autografted in second and one in third remission and two were reinduced with the protocol at first relapse. Further details are given in Table 9.

TABLE 9. PATIENT CHARACTERISTICS: ALL

PATIENTS TREATED WITH ABMT DURING 1ST REMISSION

| UPN | Sex | Age | FAB/IM CLASS. | NO. OF GRAFTS | DIAG ->CR | CR-> ABMT | DIAG-> ABMT | STATUS POST ABMT | DFS SURV. POST ABMT | TOTAL SURV. | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 57 | M | 23 | T-ALL | 1 | 1 | 3 | 4 | CR | 2 | 8 | DEAD |
| 69 | F | 24 | ALL | 2 | 1 | 4 | 5 | CR | 33 | 42 | DEAD |
| 103 | M | 16 | cALL | 2 | 2 | 6 | 8 | CR | 32 | 40+ | Relapse |
| B1 | M | 18 | cALL L1 | 1 | 1 | 10 | 11 | NE Died day 146 | 5 | 16 | DEAD |
| B2 | F | 49 | cALL L1 | 2 | 2 | 15 | 17 | CR | 24+ | 41+ | A & W |
| 150 | M | 46 | cALL | 2 | 2 | 1 | 3 | NE Died day 88 | 3 | 6 | DEAD |
| 157 | M | 22 | cALL L2 | 1 | 7 | 2 | 9 | NE Died day 23 | 1 | 10 | DEAD |
| 164 | M | 16 | ALL L2 | 1 | 1 | 3 | 4 | CR | 10 | 19+ | Relapse |

PATIENTS TREATED WITH ABMT AS REINDUCTION THERAPY OR IN 2ND OR 3RD REMISSION

| UPN | Sex | Age | FAB/IM CLASS. | NO. OF GRAFTS | DIAG ->CR | CR-> ABMT | DIAG-> ABMT | STATUS POST ABMT | DFS SURV. POST ABMT | TOTAL SURV. | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 39*/** | M | 19 | ALL | 2 | 1 | 32 | 33 | CR | 5 | 41 | DEAD |
| 51*/** | F | 35 | cALL | 2 | 1 | 58 | 59 | CR | 47+ | 106+ | A & W |
| 67* | F | 23 | ALL | 1 | 2 | 17 | 19 | CR | 7 | 28 | DEAD |
| 90 | M | 6 | T-ALL | 2 | 1 | 5 | 6 | CR | 3 | 14 | DEAD |
| 96* | M | 23 | cALL | 1 | 1 | 27 | 28 | CR | 2 | 32 | DEAD |
| 107* | M | 47 | cALL | 2 | 2 | 39 | 41 | CR | 10 | 52 | DEAD |
| 118 | F | 22 | NULL ALL | 2 | 2 | 41 | 43 | CR | 9 | 60 | DEAD |
| 121 | M | 38 | T-ALL | 2 | 2 | 30 | 32 | NE Died day 124 | 4 | 36 | DEAD |
| 135 | F | 13 | ALL | 1 | **** | **** | 31 | CR | 23+ | 54+ | A & W |
| B5*** | F | 19 | ALL L2 | 1 | 1 | 59 | 60 | CR | 5 | 68 | DEAD |

UPN = Unique Patient Number. All patients grafted in the Bloomsbury Transplant Unit have been given consecutive numbers dependent only on the date of ABMT. Where the UPN has been prefixed with a 'B' the patients were grafted at the Queen Elizabeth Hospital, Birmingham; FAB/IM CLASS = French, American, British classification together with the immunological markers where available; NO. = Number; DIAG = Diagnosis; CR = Complete remission; DFS SURV. = Disease free survival; NE = Not Evaluable.

* Patients who were harvested in 1st remission.

** Patients who were treated in 1st relapse.

*** Patient who was harvested and treated in third remission.

**** This patient had CR1 induced abroad. No information as to the time of her CR1 is available.

All time intervals are recorded as months.

+ indicates continuing survival.

BONE MARROW HARVESTING, CRYOPRESERVATION AND REINFUSION

Bone marrow was harvested, cryopreserved and reinfused as previously described (Chapter 2; Linch et al, 1982)[107]. 13 patients were harvested in CR1, 4 in CR2 and one in third remission (CR3). The mean number of nucleated cells frozen was $1.98 \times 10^8$ cells/kg body weight (range $0.68\text{-}4.04 \times 10^8$ cells/kg). The time for which the marrow was stored in liquid nitrogen before both ABMT I & II is shown in Table 10.

Table 10. Time for which marrow was stored in days: ALL

| | ABMT I | | | ABMT II | | |
|---|---|---|---|---|---|---|
| | Mean | Range | | Mean | Range | |
| CR1 | 26 | 7-108 | (n = 8) | 15 | 11-22 | (n = 4)* |
| CR2 | 44 | 9-127 | (n = 4) | 22 | 7-48 | (n = 3) |
| CR3 | 43 | | (n = 1) | | | |
| HARVEST IN CR1 TREATED AFTER RELAPSE | 682 | 412-1006 | (n = 5) | 7 | 6-9 | (n = 3) |

*One patient, UPN B2, whose ABMT II was delayed for 1 year has been omitted to prevent distortion of the mean. The marrow was stored for 361 days.

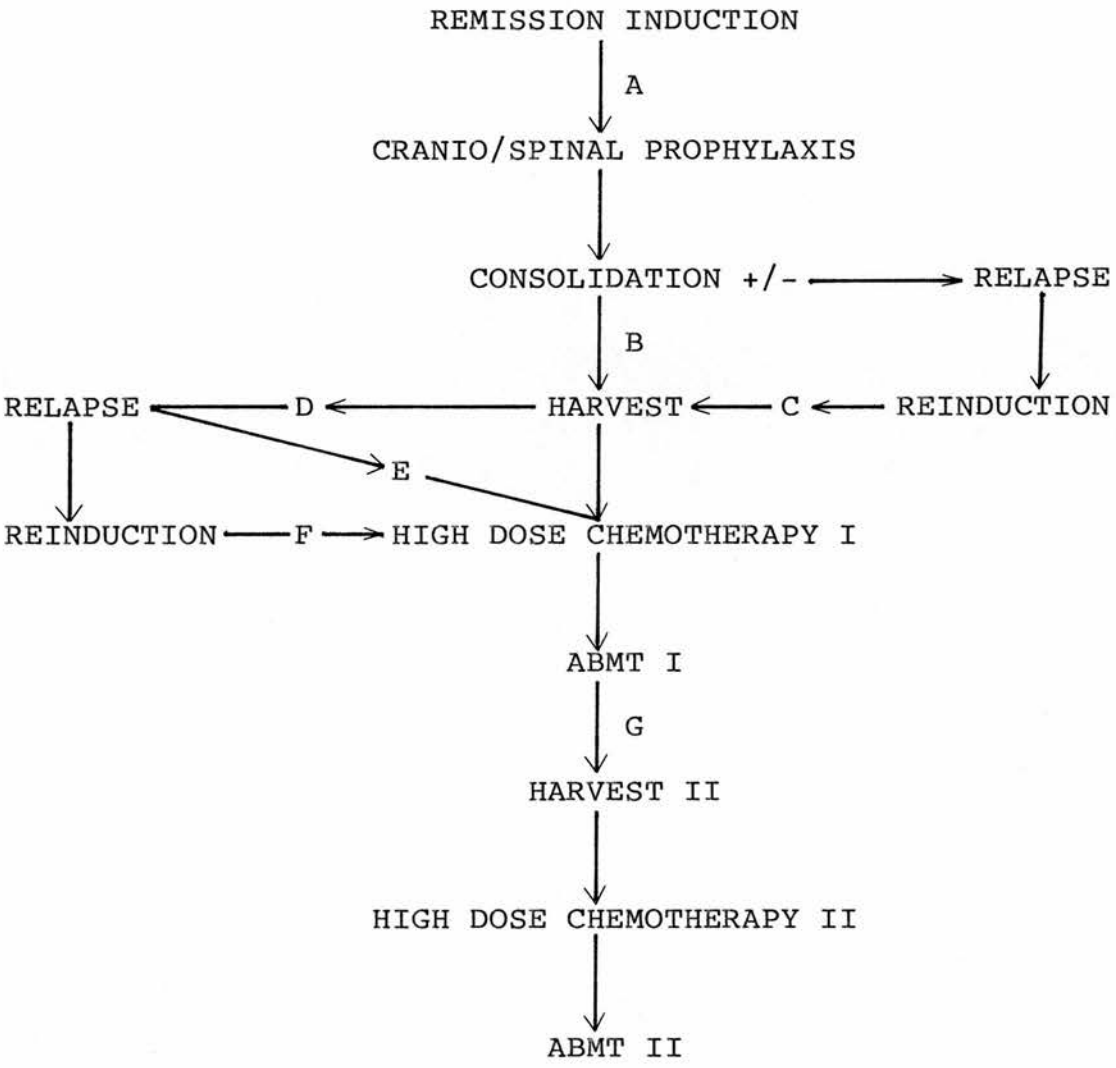
TREATMENT PLAN

The treatment plan differs from that for patients with AML; craniospinal prophylaxis is included pre-ABMT and maintenance chemotherapy is given post ABMT (Figure 9).

The first bone marrow harvest was performed, where possible, immediately following recovery from the cranio-spinal prophylaxis in first remission patients and as soon as possible following reinduction therapy in the 5 patients harvested in second or third remission.

All first remission patients were treated within 11 months of their diagnosis, mean 6 months (range 4-11).

Ten patients went on to receive a second autograft. All had their marrow reharvested as soon as possible after full haematological recovery and proceeded directly to ABMT II. The reasons for not proceeding to ABMT II are shown in Table 11.




A All patients

B 13 patients harvested in 1st remission

C 4 patients harvested in 2nd remission

D 5 patients harvested in 1st remission but not treated

E 2 patients treated in relapse

F 4 patient reinduced before treatment

G 10 patients who had ABMT II

See text for an explanation of treament regimens.

Figure 9. Treatment plan : ALL

Table 11. Reasons for not proceeding to ABMT II: ALL

| | ALL |
|---|---|
| DEATH IN PART I | 1 |
| RELAPSE | 2 (1 CNS) |
| | 1 SUSPICIOUS * |
| DELAYED HAEM. RECOVERY | 1 |
| REFUSED | 1 |
| OTHER ** | 1 |
| TOTALS | 7 |

* 1 Patient had a suspicious marrow prior to ABMT II

** 1 Patient developed pericarditis during the chemotherapy of ABMT I

HIGH DOSE CHEMOTHERAPY REGIMEN

We decided to use the same chemotherapy regimen as for patients with AML as we had already successfully treated the first two AML patients with the protocol and the cytotoxic agents used in the combination were known to be active in patients with ALL. The ablative chemotherapy used for both ABMT I and II was the same and is as follows: cyclophosphamide 1.5 G/$m^2$/day, days -5, -4 and -3, adriamycin 50 mg/$m^2$ day -5, BCNU 300 mg/$m^2$ day -5, cytosine arabinoside and thioguanine both 200 mg/$m^2$ given in two divided doses day -5 to -2 inclusive. The

autologous bone marrow was returned on day 0 (Table 12).

Table 12 UCH chemotherapy regimen for use in ABMT I & II.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE 1.5 G / $M^2$ | * | * | * | | | |
| BCNU 300 MG / $M^2$ | * | | | | | |
| CYTOSINE ARABINOSIDE 100 MG / $M^2$ | ** | ** | ** | ** | | |
| THIOGUANINE 100 MG / $M^2$ | ** | ** | ** | ** | | |
| ADRIAMYCIN 50 MG / $M^2$ | * | | | | | |
| ABMT | | | | | | * |

First remission ALL patients had both intrathecal methotrexate and cranial irradiation as CNS prophylaxis prior to ABMT.

All patients with ALL were given maintenance chemotherapy post ABMT. The regime employed combined methotrexate, mercaptopurine and cytosine arabinoside with three monthly reinduction courses of vincristine and prednisolone for at least 2 years or until relapse,

whichever was the sooner.

## RESULTS

### Response to therapy.

First remission ALL : One patient only (12.5%) remains in remission on maintenance chemotherapy 24 months post ABMT. Three patients (37.5%) died of infection, one before recovery from ABMT I, and two before recovery from ABMT II. One patient (UPN 57) with T-ALL had a CNS relapse before the second harvest and died 4 months post ABMT. Three patients have relapsed, the two who had ABMT I & II relapsed at 32 and 33 months, the third patient who only had ABMT I relapsed at 10 months post ABMT. One of the three relapsed patients (UPN 69) had an extra-medullary relapse 33 months post ABMT and died in relapse 3 months later. Both the other patients had a hypoplastic relapse, and remain alive on further chemotherapy (Figure 10).

Table 13. Response to Therapy: First Remission ALL(n = 8)

| | DFS POST ABMT (months) |
|---|---|
| 3 DIED - INFECTION | 1*, 2, 3 |
| 4 RELAPSED | 2*, 10*, 32, 33 |
| 1 REMAINS IN CCR | 24 |

* ABMT I only

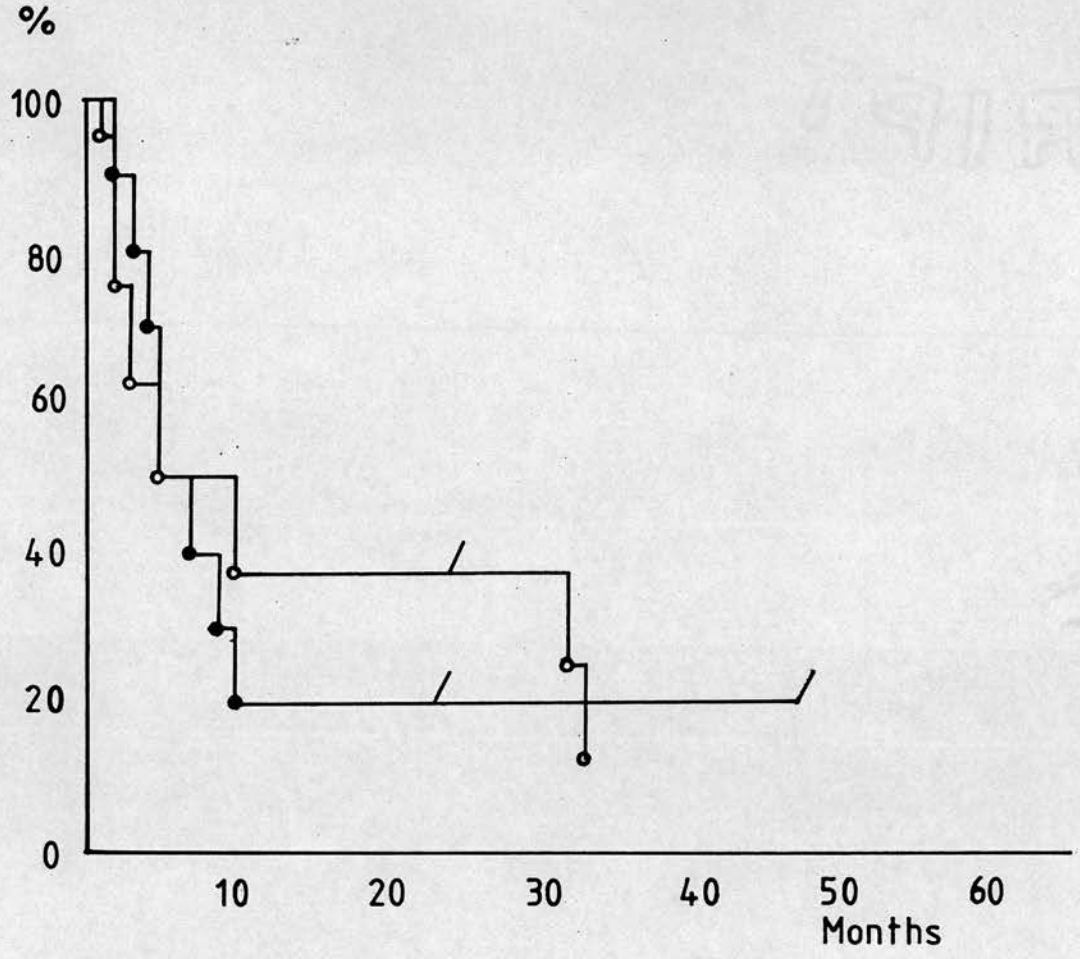



Figure 10. DFS in ALL: CR1 vs others.

Patients treated CR1 (n=8) o—o

Patients treated later than CR1 (n=10) •—•

Relapsed ALL : Two patients with ALL were treated with this regime as reinduction therapy following relapse. Both achieved a complete remission and went on to receive ABMT II. One patient (UPN 51) is still disease free in second remission 48 months post ABMT (Figure 10).

Second Remission ALL : Seven patients with ALL were treated in second remission, five have died in relapse, (4, 8, 8, 12 and 17 months post ABMT) and one died of aspergillus pneumonia day 124 during the aplasia induced by ABMT II. The remaining patient (UPN 135) continues in second remission 22 months post ABMT (Figure 10).

Third Remission ALL : One patient treated in third remission relapsed and died 8 months post ABMT (Figure 10).

Table 14. Response to Therapy: Relapsed, Second and Third Remission ALL(n = 10)

| | DFS POST ABMT (months) |
|---|---|
| 1 DIED - INFECTION | 4 |
| 7 RELAPSED | 2*, 3, 5, 5*, 7*, 9, 10 |
| 2 REMAIN IN CCR | 23*, 47 |

* ABMT I only

DISCUSSION

Autologous bone marrow transplantation for ALL in relapse is the most likely situation in which purging might be beneficial. There is as yet no evidence that purging improves survival post ABMT (Gorin et al, 1985)[79]. The European Bone Marrow Transplant Group (EBMTG) data did however, suggest that there was a survival advantage for patients with ALL treated in CR2 who had their marrow purged, but it failed to reach statistical significance and still fails to do so even after a further year of follow-up (Gorin & Aegerter, 1986)[80]. We do not use 'in vitro' purging but feel that repeating the procedure a second time should reduce the leukaemic burden further and effect 'in vivo' purging.

The relapse rate after allogeneic transplantation has been reported to be higher than 50% (Sanders et al, 1985)[150] and where it has been possible to do so, this has generally been demonstrated to be of the original host type. This suggests that failure to eradicate host disease is the likely cause. Santos et al, 1986[155], have used a higher dose of cyclophosphamide, 50 mg/kg x 4, and TBI administered in four fractions to a total dose of 12 gray. They report only one out of 39 patients treated in CR1 and CR2 to have relapsed with median follow-up of 24 months. Patients transplanted in CR3 with the same conditioning regimen had a relapse rate of 35%.

It will be very difficult to assess the contribution of purging in autografted patients in view of the many different conditioning regimens employed. It is likely that any benefit from purging will only become apparent when there is a randomised trial of patients given purged and unpurged marrow.

First remission ALL: The results of treating patients in first remission with our double ABMT protocol are strikingly different from the results of treating patients with AML in first remission, although the protocols are the same (Figure 11).

Only one patient with ALL treated in CR1 remains in CR 24 months post ABMT. The numbers of patients with ALL treated in CR1 is small, but the reason for the failure of our protocol appears two fold. Firstly, as might have been predicted from the allograft figures (Thomas et al, 1983)[175], there has been a high relapse rate, four of five patients who survived the procedure. Secondly, whereas there have been no transplant related deaths in patients with AML treated in CR1 there have been three (37.5%) such deaths in the eight patients with ALL treated in CR1. I suspect this may be related to the inclusion of steroids and craniospinal prophylaxis in the induction regimens used pre-ABMT in patients with ALL. This difference is discussed further in Chapter 8: morbidity. Clearly, our current approach to the treatment

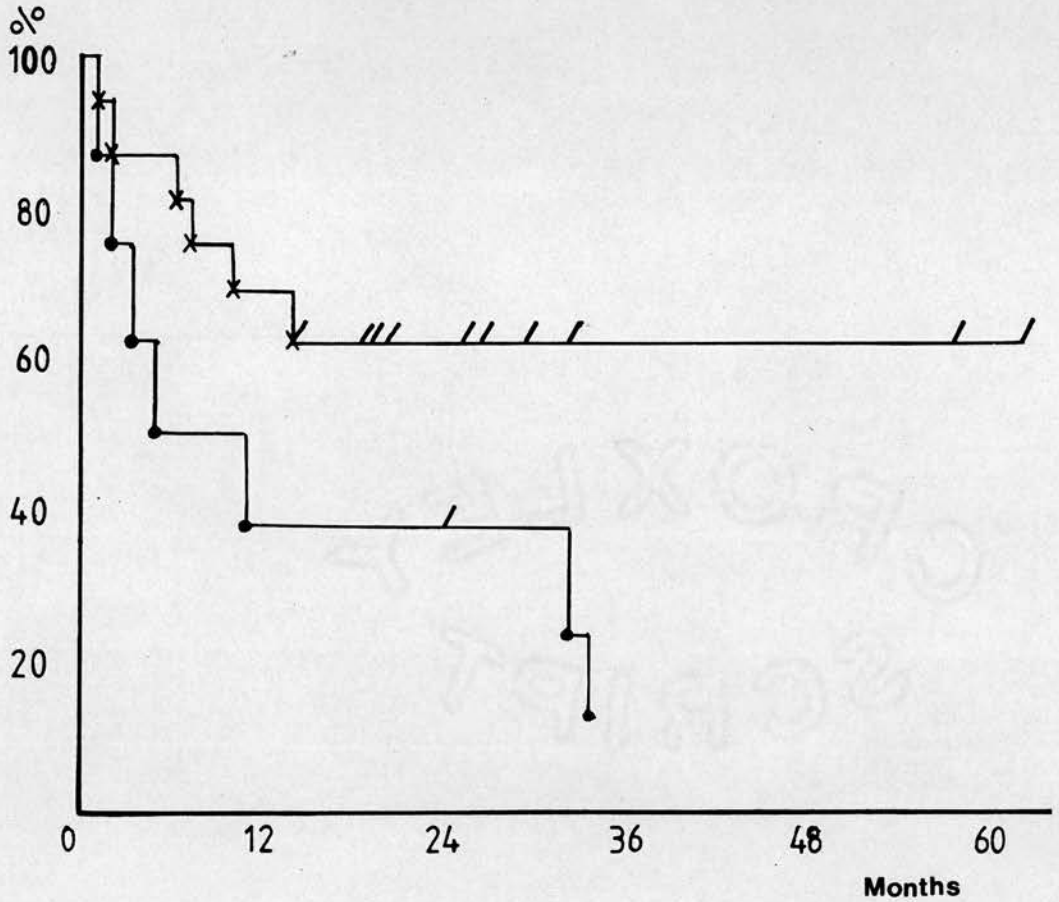



Figure 11. DFS in CR1: AML vs ALL.

AML (n=16)

ALL (n=8)

of patients with ALL in CR1 requires modification.

Five patients with ALL, received a double autograft in first remission, only one remains alive and disease free 24 month post ABMT, two died procedural deaths and two have relapsed at 32 and 33 months post ABMT, one has died and one remains alive on further therapy.

Relapsed patients with ALL: Massive chemotherapy with ABMT rescue was effective at inducing a CR in the two relapsed patients treated with the regimen. Ten of our patients were treated in relapse or second or third remission, one died a procedural death, seven have relapsed again within 10 months (2, 3, 5, 5, 7, 9 and 10 months) and all have died. Two remain in CR, 22 and 48 months post ABMT, the first patient had ABMT I only and the second ABMT I & II. Both these patients had an initial CR of >18/12 duration and would therefore fall into a better prognostic group as suggested by Rivera et al, 1986[144].

These results are poor and very similar to our results in relapsed patients with AML (Figure 12).

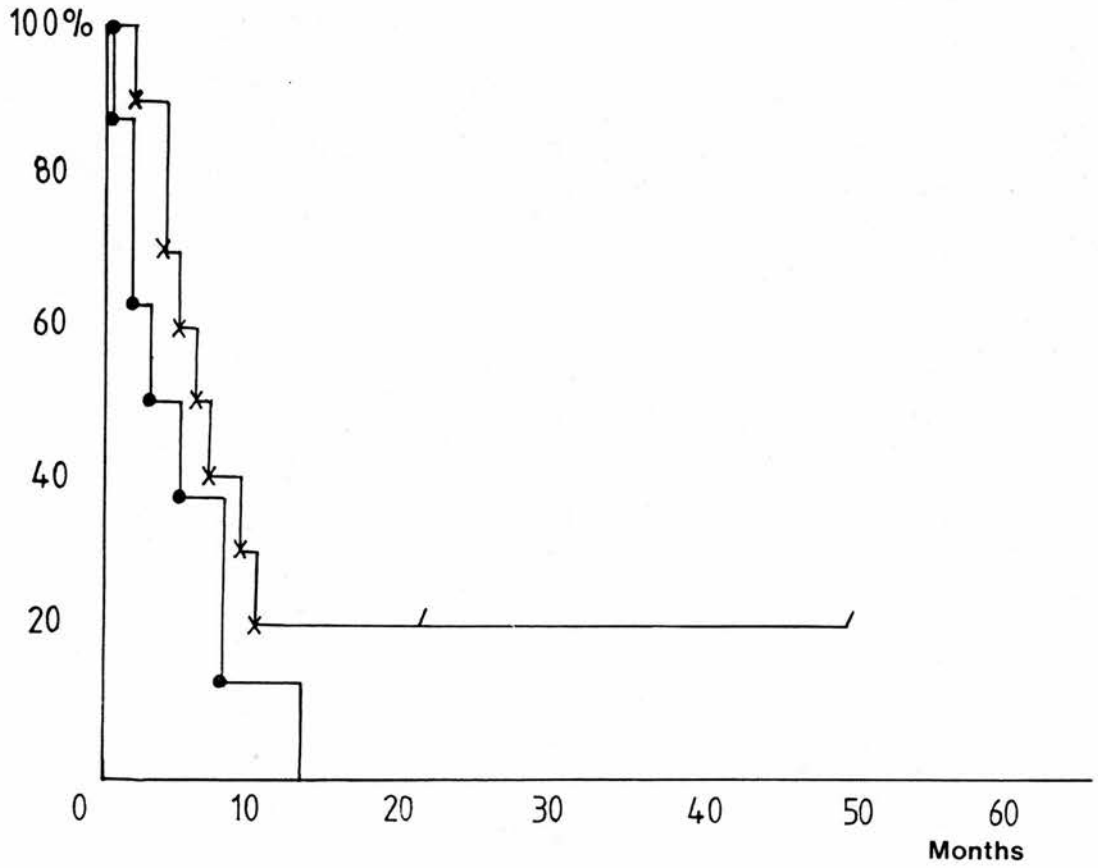



Figure 12. DFS in patients treated after CR1: AML vs ALL.

AML (n=8)

ALL (n=10)

Although our protocol appears to have been particularly unsuccessful in patients with ALL, the EBMTG data are much more hopeful. DFS for patients following ABMT in CR1 is 48% at 3 years, with no difference in DFS for patients treated in CR1 or CR2. 79% of these patients had received regimens including TBI (Gorin & Aegerter, 1986)[80].

# CHAPTER 5

## NON-HODGKIN'S LYMPHOMA

### INTRODUCTION

The non-Hodgkin's lymphomas (NHL), are a heterogenous group of disorders which, in the majority of instances are disseminated neoplasms at the time of diagnosis and are therefore not amenable to curative radiotherapy. After surgical staging, stages I and II are infrequent, except for the 'histiocytic' NHL's where approximately 30% are localized at the time of presentation (Chabner et al, 1977)[40]. Actuarial survival rates at 6 years reported by Bush et al, 1977[32], for Stages I and II treated by curative radiotherapy for all histologies were 70 and 60% respectively.

There are many pathological subtypes but an early successful attempt to classify the NHL's by Rappaport, 1966[135] divided patients with NHL into two prognostic categories: 'favourable' prognosis histology wherein the median survival will be in excess of 5 to 7 years and 'unfavourable' prognosis where the median survival is less than 2 years and often less than 1 year. This has enabled clinical trials of various investigational

treatments to be compared. However, there is still no universally accepted histological classification of the NHL's. The most recent attempt to arrive at an internationally acceptable classification is the working formulation of the NCI group (Rosenberg et al, 1982)[146] which divided them broadly into 3 categories: low, intermediate and high grade histology again reflecting their prognosis.

The optimum treatment of low grade or good prognosis NHL is not clear in view of their relatively indolent course and long-term survival.

The intermediate and high grade NHL have been treated with a variety of combination regimens, with some success eg. COP-BLEO 59% CR rate, CHOP 59% CR rate in all histologies (Jones et al, 1979; McKelvey et al, 1976; Skarin et al, 1978)[96,119,159]. However, within these groups, patients with advanced diffuse 'histiocytic' lymphoma, according to the histological classification of Rappaport (1966)[134] did less well. The use of MOPP in this group of patients with diffuse histiocytic lymphoma was reported by DeVita et al, 1975[51], to achieve a CR in 41% with long-term disease free survival being the rule in those achieving a CR. All studies demonstrate that the achievement of a CR is the most important factor for long-term survival. Treatment after relapse has occurred produces less good CR rates and the duration of remission

is very limited (Cabanillas et al, 1978; Herrmann et al, 1981)[33,87]. Consequently the present treatment of the patient with a high grade NHL is with increasingly intensive chemoradiotherapy regimens designed to produce a CR and hopefully long-term survival.

More intensive regimens without marrow rescue have been reported to have been employed as first line therapy in patients with advanced poor prognosis histology NHL groups: high dose adriamycin and cytosine arabinoside (Dabich et al, 1985)[45], F-MACHOP (Amadori et al, 1985)[3], ProMACE-MOPP (Fisher et al, 1985)[66], MACOP-B (Klimo & Connors, 1985)[101]. These regimens appear to result in 80%+ CR rates with long-term disease free survival in the majority of patients achieving a CR, resulting in a median survival in excess of 4 years. These studies were small pilot studies in tertiary referral centres and up to 39% of patients treated had stage II disease. Patients with initial CNS disease and those judged to have cardiac, liver or renal disease, were excluded from one of the studies. Another of the studies excluded 2 patients dying in the first week from their final analysis. Nonetheless, ABMT used as consolidation therapy must now be compared with these first line regimens and not compared with historical controls. Proper comparison would need to be in a randomised controlled trial. Similarly the success of intensive chemoradiotherapy regimens with ABMT in relapsed patients must be

considered in relation to previous chemotherapy +/- DXT that the patient has already received and then compared with the best currently available salvage regimen when used in relapsed patients with comparable prior treatment eg. IMVP-16 (Ifosphamide (I), Methotrexate (M), Etoposide (VP-16)(Cabanillas et al, 1982)[34].

Cabanillas et al, 1982 [34], used IMVP-16 in 52 patients with lymphoma who had failed to attain an initial remission or had relapsed. 32 patients (62%) responded (CR 37%, PR 25%). The projected median survival of the complete responders is 15 months. All relapses have occurred within 12 months. 2 patients died of sepsis related to myelosuppression induced by the regime.

It is in an effort to improve the response rate and prolong survival that we have employed massive doses of chemotherapy with autologous bone marrow rescue in patients with NHL who fail to enter CR or relapse after initial chemotherapy.

PATIENTS

Twenty-one patients with non-Hodgkin's lymphoma, have been treated between September 1981 and September 1985 with this form of therapy. They were all adults (14 males, 7 females), with a median age of 41 years (range

19-66 years). 11 patients had received more than one chemotherapy regime and all had received anthracycline-containing combinations. 10 patients had also received radiotherapy. For the purposes of classification of disease at the time of grafting 'resistant relapse' (RR) indicates that the patient had progressive disease in spite of conventional chemotherapy whilst 'non resistant relapse' (NON RR) indicates that the patient although relapsed was still responding to either second, third or fourth line therapy, or that the high dose chemoradio-therapy regime was employed as the second line regime at the time of relapse. Histological classification is by the NCI sponsored working formulation (Rosenberg et al, 1982)[146]. Further details are given in Table 15.

TABLE 15. PATIENT CHARACTERISTICS : NON-HODGKINS LYMPHOMA

| UPN | Age | Sex | HIST CLASS ST @ DIAG | DIAG ->ABMT | PREVIOUS TREATMENT | STATUS AT ABMT | ABMT CHEMO | STATUS POST ABMT | DFS | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|
| 34 | 38 | M | INT / III | 28 | CHOP<br>M BACOD | RR | UCH I&II | CR | 7 | DEAD 8 |
| 65 | 39 | M | INT / IV | 10 | CHOP X 7<br>BACOP<br>M BACOP | RR | UCH I&II | PR | | A & W 42+ |
| 75 | 49 | M | HIGH / IIB | 11 | CHOP<br>HD MTX<br>DXT | RR | UCH I | NE | | DEAD day 9 |
| 94 | 50 | M | INT / II | 21 | ORCHIDECT<br>CHOP X 6 | NON RR | UCH I | CR | 9 | DEAD 11 |
| 101 | 47 | M | INT /<br>CONJUNCTIVAL | 46 | CHOP X 6<br>DXT | NON RR | UCH I&II | PR | | REL 28+ |
| 102 | 28 | F | INT | 10 | CHOP X 3<br>HD MTX X 4<br>DXT | RR | UCH I | NR | | DEAD day 33 |
| 114 | 29 | M | INT / MES<br>MASS | 6 | CHOP X 4<br>EVAP X 1 | RR | UCH I | NR | | DEAD day 44 |
| 126 | 21 | M | HIGH / MED<br>MASS | 10 | CHOP X 4<br>Cyt/Thio/<br>Cyclo X 1<br>IT MTX &<br>DXT | RR | BEAM | NR | | A & W 26+ |
| 133 | 41 | M | INT / II | 4 | CHOP X 2 | RR | BEAM | NR | | DEAD 3 |
| 136 | 19 | M | HIGH / I | 10 | DXT<br>M BACOD X 4 | RR | BEAM | NR | | DEAD day 50 |
| 137 | 45 | F | INT / I | 39 | CHOP X 6<br>M BACOD X 4<br>DXT X 2 | RR | BEAM | NR | | DEAD 2 |
| 153 | 33 | F | HIGH / IVB | 12 | CHOP X 6<br>Cis Plat X 1 | NON RR | BEAM | CR | 2 | DEAD 8 |
| 158 | 50 | M | INT / IVA | 10 | CHOP X 6 | NON RR | BNLI | PR | | DEAD 7 |
| 161 | 47 | M | INT / 1<br>JEJUNUM | 7 | CHOP | NON RR | BNLI | NE | | DEAD day 15 |
| 166 | 21 | M | HIGH / | 8 | LOPP X 3<br>EVAP X 1<br>VIND/VP16/<br>CCNU/DEX<br>DXT X 2 | RR | BNLI | NE | | DEAD day 3 |
| 168 | 56 | F | HIGH / IVA | 15 | CHOP X 7 | NON RR | BNLI | NE | | DEAD day 5 |
| 183 | 39 | F | HIGH / IV | 10 | CHOP X 6<br>DXT | NON RR | BNLI | CR | 4 | REL 9+ |
| 187 | 50 | M | HIGH / III | 21 | ProMACE/<br>MOPP | NON RR | BEAM | CR | 7+ | A & W |
| 191 | 30 | F | | | | NON RR | BNLI | CR | 6+ | A & W |
| 195 | 45 | F | INT / IIA | 29 | COP X 4<br>MBACOD X 4<br>DXT | NON RR | BEAM | CR | 6+ | A & W |
| 196 | 66 | M | HIGH / II<br>( + CNS ) | 17 | ORCHIDECT<br>MBACOD X 6<br>DXT(CRANIAL)<br>IT MTX X 10 | NON RR | TBI/CYCLO | CR | 1<br>CNS | REL 5+ |

Legend Table 15: UPN = Unique patient number; HIST CLASS = Histological classification; INT = Intermediate grade diffuse; HIGH = High grade diffuse; ST @ DIAG = Stage at diagnosis (This refers to the Ann Arbor staging classification); DIAG -> ABMT = The time interval between diagnosis and ABMT; PREVIOUS TREATMENT: CHOP = Cyclophosphamide, Adriamycin, Vincristine, Prednisolone; M BACOD = Methotrexate, Bleomycin, Adriamycin, Cyclophosphamide, Vincristine, Dexamethasone; BACOP = Bleomycin, Adriamycin, Cyclophosphamide, Vincristine, Prednisolone; M BACOP = Methotrexate, Bleomycin, Adriamycin, Cyclophosphamide, Vincristine, Prednisolone; HD MTX = High dose methotrexate; DXT = Radiotherapy; EVAP = VP16, Vinblastine, Adriamycin, Prednisolone; Cyt/Thio/Cyclo = Cytosine Arabinoside, Thioguanine, Cyclophosphamide; IT MTX = Intrathecal methotrexate; MOPP = Nitrogen Mustard, Vincristine, Procarbazine, Prednisolone; LOPP = Chlorambucil, Vincristine, Procarbazine, Prednisolone; Cis Plat = Cis Platinum; VIND /VP16/CCNU/DEX = Vindesine, VP16, Lomustine, Dexamethasone; ProMACE = Prednisolone, Methotrexate, Adriamycin, Cyclophosphamide, VP16; COP = Cyclophosphamide, Vincristine, Prednisolone; ORCHIDECT = Orchidectomy; STATUS AT ABMT: RR = Resistant Relapse; NON RR = Non Resistant Relapse; ABMT CHEMO = ABMT Chemotherapy; STATUS POST ABMT: CR = Complete Remission; PR = Partial Remission; NE = Not Evaluable; NR = No Response; DFS = Disease Free Survival; CURRENT STATUS: A & W = Alive and Well; REL = Relapse; All time intervals are months unless otherwise stated.

## BONE MARROW HARVESTING, CRYOPRESERVATION AND REINFUSION

Bone marrow was harvested, cryopreserved and reinfused as previously described (Chapter 2; Linch et al, 1982)[107].

Bone marrow was harvested at relapse in 18 cases and during CR1, CR2 and CR3 respectively in the remaining three cases. Only one patient was known to have had marrow involvement at some stage prior to her bone marrow harvest. The mean number of nucleated cells frozen per kg body weight was $1.64 \times 10^8$ cells/kg (range $0.36-2.4 \times 10^8$ cells/kg). The marrow was stored in liquid nitrogen for a median of 12 days (range 6-572 days) between harvesting and reinfusion of the first aliquot.

## TREATMENT PLAN

The treatment plan varied depending on the treatment regimen to be employed. If the UCH double protocol was employed then only one marrow harvest was performed and providing that more than $1.2 \times 10^8$ nucleated cells/kg body weight were obtained post processing, the harvested marrow was divided and half given after each course. UCH II was given as soon as there was haematological recovery from UCH I. Seven patients received UCH I but only 3 received UCH I & II. Three of the patients did not continue to UCH II because of septicaemic death following

UCH I (UPN 75) or rapid progression of disease (UPN 102 & 114). One patient who attained a CR after UCH I, declined UCH II. The BEAM and BNLI protocols were used as single ABMT protocols.

## HIGH DOSE CHEMOTHERAPY REGIMENS

Three separate chemotherapy regimens were used, UCH I & II, BEAM and the BNLI protocol. UCH I & II was a two cycle regime designed to introduce as many new, potentially non-cross-resistant drugs as possible. UCH I was based on the UCH double protocol for patients with acute leukaemia (Table 16).

The adriamycin was dropped from the protocol as it was argued that all patients would have received it already, and its inclusion at conventional dosage would therefore only serve to increase the toxicity of the regimen without additional anti-tumour benefit. It was also assumed that the patients general condition would be worse than the leukaemic patients who were generally treated during remission. For UCH II methotrexate was added instead of the cyclophosphamide, it was to be used at high dose with folinic acid rescue. This drug has since been used at much higher dosage without ABMT rescue, and indeed, the UCH II regimen proved much less myelotoxic in the three patients who received it, than

did UCH I.

Table 16. UCH double protocol for AML.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE | * | * | * | | | |
| 1.5 G / $M^2$ | | | | | | |
| BCNU | * | | | | | |
| 300 MG / $M^2$ | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | |
| 100 MG / $M^2$ | | | | | | |
| THIOGUANINE | ** | ** | ** | ** | | |
| 100 MG / $M^2$ | | | | | | |
| ADRIAMYCIN | * | | | | | |
| 50 MG / $M^2$ | | | | | | |
| ABMT | | | | | | * |

The regimen was as follows: UCH I : Cyclophosphamde 4.5 g/$m^2$, BCNU 300 mg/$m^2$, Cytosine Arabinoside 800 mg/$m^2$; UCH II : Methotrexate 1 g/$m^2$ with folinic acid rescue, BCNU 300 mg/$m^2$, Cytosine Arabinoside 800 mg/$m^2$ (Table 17).

Table 17. UCH I & II.

| UCH I | DAY 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE | * | * | * | | | |
| 1.5 G / $M^2$ | | | | | | |
| BCNU | * | | | | | |
| 300 MG / $M^2$ | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | |
| 100 MG / $M^2$ | | | | | | |
| ABMT | | | | | | * |

| UCH II | | | | | | |
|---|---|---|---|---|---|---|
| METHOTREXATE | * | | | | | |
| 1.0 G / $M^2$ | | | | | | |
| BCNU | * | | | | | |
| 300 MG / $M^2$ | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | |
| 100 MG / $M^2$ | | | | | | |
| ABMT | | | | | | * |

The BEAM regime was employed as a single therapeutic procedure. The regimen was adopted as a collaborative protocol with other European centres, in the hope of accruing sufficient numbers of patients so as to enable a rapid assessment of the worth of this form of therapy. The regimen is as follows: BCNU 300 $mg/m^2$ and cytosine arabinoside 800 $mg/m^2$ were common to UCH I. Melphalan 140

mg/$m^2$ was used in BEAM instead of the cyclophosphamide 4.5 g/$m^2$ in UCH I. BEAM also contains VP16 400 mg/$m^2$ (Table 18).

Table 18. BEAM protocol.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| BCNU | * | | | | | | |
| 300 MG / $M^2$ | | | | | | | |
| VP16 | ** | ** | ** | ** | | | |
| 50 MG / $M^2$ | | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | |
| MELPHALAN | | | | | | * | |
| 140 MG / $M^2$ | | | | | | | |
| ABMT | | | | | | | * |

The BNLI protocol (Table 19) is the protocol adopted by the British National Lymphoma Investigation in protocol C of their current study of generalised grade II NHL (BNLI NHL GEN GDII 85)[25].

Table 19. BNLI protocol.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE | * | * | * | * | | | |
| 1.5 G / $M^2$ | | | | | | | |
| BCNU | * | | | | | | |
| 300 MG / $M^2$ | | | | | | | |
| VP16 | * | * | * | * | | | |
| 75 MG / $M^2$ | | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | |
| ABMT | | | | | | | * |

The objectives of the study are: 1. To determine, in patients with Stage III/IV NHL without bone marrow involvement, the CR rate using highly intensive chemotherapy with ABMT in those patients not in CR after 3 courses of CHOP. 2. To determine whether high dose chemotherapy and ABMT can produce prolonged DFS in those patients who have not completely responded to 3 courses of CHOP. 3. To assess the value of high dose chemotherapy and ABMT as initial salvage therapy in those patients relapsing after CHOP therapy. It consists of the same agents as in UCH I together with the addition of VP 16. Details of the dose variations are given in Table 15. The first patients we treated with this protocol were generally patients with more advanced disease and not

eligible for entry into the BNLI trial.

## RESULTS

### Response To Therapy

Response to therapy was evaluated both clinically and by repeat computed axial tomography (CAT) scanning where previously abnormal. A complete remission was defined as the complete resolution of all signs and abnormal investigations in patients surviving beyond 30 days.

Of 21 patients with NHL 8 (39%) achieved a CR and 3 (14%) a PR. In 2 of these patients with a PR, there was a clinical CR but the repeat CAT scans showed a residual mass in the abdomen. One of these patients (UPN 65) was given 29.80 gray DXT post ABMT, to the abdominal mass which had no effect as judged by further CAT scanning. This patient however remains alive and well 42 months post ABMT. The other patient (UPN 101) was given no further treatment at this stage. At day 263 a laparotomy and cholecystectomy were performed following an episode of cholecystitis. Splenectomy and multiple para-aortic and mesenteric node biopsies showed no disease. However, a biopsy from retroperitoneal tissue near the base of the left ureter showed a lymphocytic infiltration, strongly suggestive of lymphoma. The patient was then treated

with para-aortic irradiation and further chemotherapy. He continues alive in remission 32 months post ABMT. The third patient (UPN 158) had generalised residual disease and died 5 months post ABMT in spite of further chemotherapy. There was no response in six patients. Four patients were non-evaluable, two because of death from septicaemia at day 9 and 15, and two because of death due to either tumour progression or drug toxicity at day 3 and 5. Of 11 responding patients 5 are still alive 42, 32, 7, 6, and 6 months post ABMT.

One further patient (UPN 126) was treated with ABMT when thought to have failed induction therapy with CHOP x 4, because a CAT scan showed a residual mass in the mediastinum. A repeat CAT scan post ABMT showed no change. He was therefore given boost DXT to the mediastinum. Over the next few months the mass shrank. He has therefore been classified as a non-responder but he remains well with no other evidence of disease and on no treatment 25 months post ABMT.

## DISCUSSION

Appelbaum et al, 1981[6], used high dose chemoradiotherapy followed by syngeneic bone marrow transplantation in 8 patients with disseminated NHL who failed conventional combination chemotherapy. 7 achieved a CR, 2

have relapsed and one died of Pseudomonas pneumonia whilst still in CR. 4 remained in CR at the time of reporting, 12, 21, 32 and 126 months post transplant. Appelbaum et al, 1983[7], following the success of intensive chemoradiotherapy and a syngeneic graft used allogeneic transplantation in 20 patients with intermediate and high grade NHL's who had failed on conventional chemotherapy regimens. There were 14 CR's, 4 NR's and 2 early transplant related deaths. 4 patients remain in CR at 6, 8, 27 and 65 months, 4 have relapsed and 6 further patients have died of transplant related complications.

Phillips et al, 1984[130], reported the use of high dose cyclophosphamide and TBI followed by ABMT in 27 patients with malignant lymphoma; 24 NHL: 3 HD. 15 patients achieved a CR (56%) 5 of whom remain in CR 19-71 months post ABMT. There were 6 transplant related deaths 3 from interstitial pneumonitis, 2 from sepsis and one due to congestive cardiac failure.

Verdonck et al, 1985[179], used a similar regimen with ABMT in 14 patients. 8 of whom had relapsed or had primary resistant disease and 7 of these attained a CR. The remainder were patients with a bad prognosis who were treated as consolidation during first or second CR. Only one of the patients treated for relapsed or resistant disease remains in CR at 28 months, one died of sepsis

and the others of recurrent lymphoma. 5 of the patients treated as consolidation remain in CR 7-31 months post ABMT. The other patient died of acute myeloid leukaemia which may have been secondary to his previous treatment. This series demonstrates not only less toxicity for ABMT than allografting but also a possible benefit from using the treatment earlier in the course of the disease in fitter patients.

Our early results in this study demonstrated that in patients with lymphoma resistant to conventional therapy, very high dose chemotherapy could still produce significant responses and even complete remission in some cases. These responses were not in general sustained. We have therefore tried to use the very high dose chemotherapy regimes earlier in the course of the disease. The success of this strategy can best be demonstrated by comparing the results of patients regarded as being in resistant relapse (RR) with those treated whilst still thought to be responding (non-resistant relapse, NON RR). 10 patients classsified as being in RR were treated with our intensive chemotherapy regimes followed by ABMT and only 1 achieved a CR and 1 a PR, there were 6 non-responders and 2 early deaths. We have treated 11 patients regarded as having a poor prognosis with the high dose chemotherapy when they were still responding to conventional therapy, NON RR, and they have an improved response rate. Two of the eleven

patients treated died septicaemic deaths, but of the 9 evaluable patients, 7 achieved a CR and 2 a PR (Figure 13). These patients are only recently treated with the protocol and whether the treatment will produce long-term survivors or even longer survival than the previous more conventional protocols cannot yet be assessed.

The ability of this type of treatment to prolong DFS may be assessed by considering the outcome in the first 12 patients we treated with the UCH I and II, and BEAM protocols. There was a total of 3 CR's and 2 PR's. The 3 CR's relapsed 2, 7 and 9 months post ABMT and are now dead. Of the 2 patients designated as PR because of apparent residual abdominal disease on CAT scanning, one patient (UPN 65), who received boost DXT post ABMT and no further treatment, remains alive and well 42 months post ABMT and the other patient (UPN 101) has had a laparotomy at which residual disease was detected but he continues well after further treatment 28 months post ABMT. The patient treated as a CHOP failure in this group (UPN 126) and designated NR because of no change on the CAT scan post ABMT, received boost DXT to the mediastinum with gradual resolution of the residual mass over the following months, he remains well on no treatment 26 months post ABMT. It is sometimes difficult to determine, with CAT scanning, whether a residual mass represents tumour or inflammatory and fibrotic tissue.

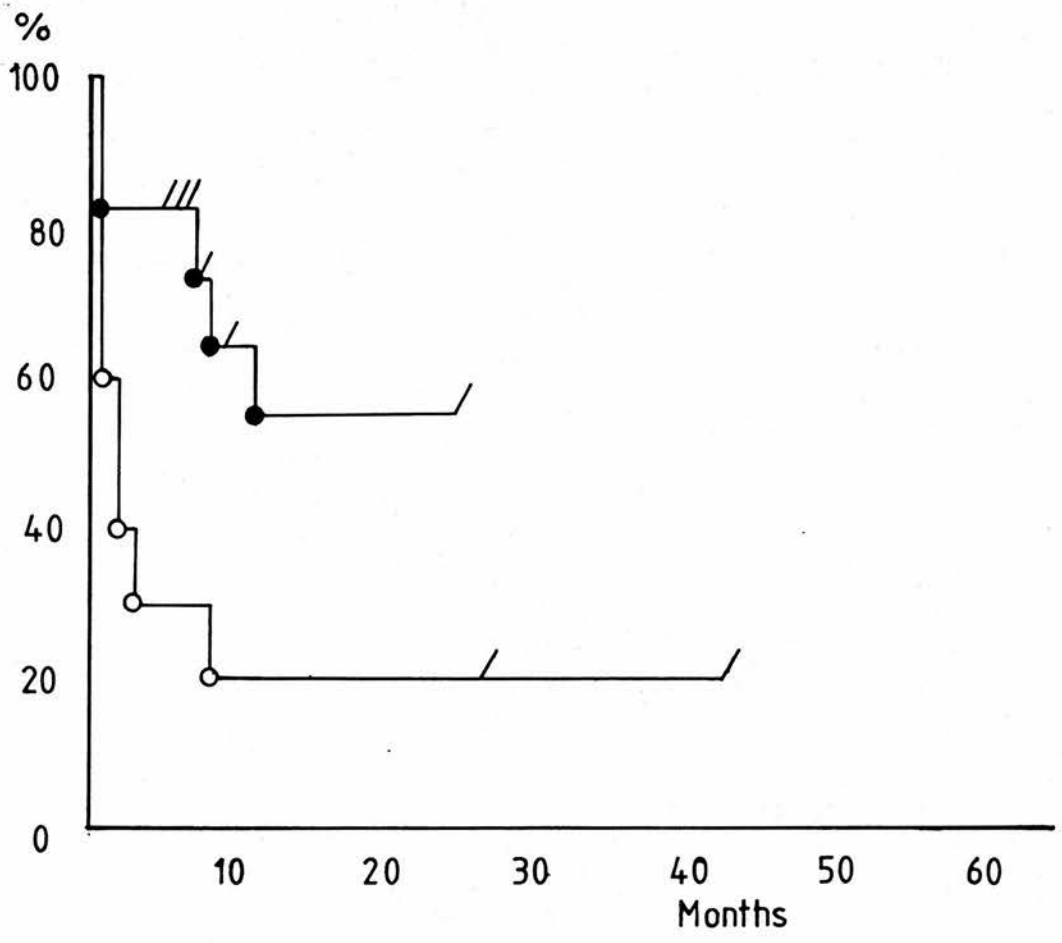



Figure 13. Survival in NHL: RR vs NON RR.

RR (n=10)

NON RR (n=11)

In the 9 patients treated since then, 8 patients although relapsed have been treated with the protocol as second or third line therapy, where DXT had already been employed. Only one was a patient with resistant relapse. There were 5 CR's, 2 have already relapsed day 41 (CNS relapse) and day 118, the three others remain in CR 6, 6 and 7 months post ABMT. One patient who only acheived a PR has already died of disease 7 months post ABMT. Three of the patients were non evaluable because of early deaths.

The morbidity in this series has been high. To improve upon these results it will be necessary to proceed to ABMT at an earlier stage in the disease process when the patients are in better clinical condition and have less resistant disease. This strategy of bringing forward high dose therapy to an earlier stage of the disease has been successful for allogeneic bone marrow transplantation in AML (Thomas ED, 1983)[169], but the situation is more complex for the lymphomas. Unlike AML some patients with NHL, can be cured by much safer initial therapy. It is therefore important to try and define patients with a poor prognosis. In the disseminated Stage III/IV NHL with aggressive histology, those patients not in CR after 3 courses of CHOP have a very poor prognosis with <10% long-term survivors, (BNLI CHOP study - unpublished data) and such patients should be considered for alternative therapy such as ABMT at this stage. We have only used

intensive chemotherapy with ABMT rescue in one such patient who had minimal morbidity from the procedure, achieved a CR and is now 6 months post ABMT on no therapy. Her results are not included further in this report. In the study reported by Philip et al, 1983 [101], it should be noted that whereas all 4 patients treated with resistant disease died within 90 days, 5 out of 9 patients grafted because of early failure to obtain a CR or in a second complete remission, are alive at 100-900 days.

In this and other studies of autologous bone marrow transplantation in lymphoma (Philip et al, 1983; Phillips et al, 1984)[128,130] the marrows were not infiltrated as determined by morphological criteria, but clearly the presence of occult disease cannot be excluded. This anxiety has prompted some groups to 'purge' the harvested bone marrow of potentially malignant B cells in cases of B cell NHL (Nadler et al, 1984)[122]. However, in this study and that of Phillips et al, 1984[130], the main cause of failure in patients with NHL, was primary resistance to the high dose therapy used, and in those responding patients who relapsed, the relapses were mainly localized to a site of previous lymphomatous involvement.

This study thus shows that in patients with advanced relapsed NHL, resistant to conventional dosage chemotherapy very high dose chemotherapy and ABMT may

still produce a significant anti-tumour response. The morbidity and relapse rate have been high and it is clear that future studies of very high dose chemoradiotherapy must be directed at poor prognosis patients in an earlier stage of their disease.

# CHAPTER 6

## HODGKIN'S DISEASE

### INTRODUCTION

Localized Hodgkin's disease (HD) is today a disease that is curable by radiotherapy in the majority of cases (Weller et al, 1976)[185] even a fair proportion of patients presenting with advanced HD will be cured by combination chemotherapy (DeVita et al, 1980)[52]. In 1954, however, HD was still described as "a progressive condition leading inexorably to death" (Lumb GD)[111]. As early as 1922, Gilbert[72] began to administer increased doses of radiation, not only to involved lymph node chains but to cover entire chains not obviously involved by the disease and he reported long-term survival without recurrence in a few cases. Both his and similar reports (Baker & Mann, 1939; Slaughter & Craver, 1942)[11,161] which also appeared in the literature after surgical extirpation or surgery and radiotherapy were not accepted as cures because of the recognition of isolated cases of HD which can pursue an unusually benign course consistent with survival for many years (Stout AP,1949)[165].

Jelliffe & Thomson (1955)[94], Peters & Middlemiss

(1957)[127], Kaplan HS (1962)[99] and others demonstrated a dose-response curve for radiation therapy in HD. Kaplan's study at Stanford University established that doses in excess of 3,600 and less than 4,500 rads could cure most patients with stage IA and IIA disease and this observation has been confirmed in many later studies. Much of the advance in treating HD with radiotherapy was made possible by the improvements in radiotherapy equipment and techniques.

Various compounds including iron, arsenic, vitamins and cod-liver oil had been used in the treatment of HD since 1823 (Hoster & Dratman, 1948)[92] but none had consistently improved the disease. In 1946, Goodman and associates[76] reported the first clear evidence of response in some patients with advanced HD when treated with nitrogen mustard. DeVita et al, 1965[49] were the first to use four agents in the management of advanced HD. They reported an 80% complete response rate for the combination of nitrogen mustard, vincristine, methotrexate and prednisone (MOMP)in a single cycle. From this pilot study they went on to develop the MOPP combination (DeVita et al, 1970)[50] in which methotrexate was replaced by procarbazine. Patients were treated with 6 cycles and then followed in unmaintained response. The initial complete response rate was 81% and at the time of initial reporting the median duration response was not reached but likely to be between 29-42 months and the

median survival had not been reached with a minimum follow up of 32 months. This represented a monumental turn of events in the treatment of advanced HD where after 6 months of chemotherapy 47% of those at risk for four years had been continuously free of disease. These results have now been confirmed in many other centres (Frei et al, 1973; Case et al, 1977)[68,39] and no other combination has yet been produced which demonstrates significantly better results (Bonadonna et al, 1975; McElwain et al, 1977)[20,118].

Frei et al, 1973[68] not only confirmed the early MOPP results in patients with advanced HD but randomized patients who achieved a complete response to one of two treatment arms. One received no maintenance after 6 cycles of MOPP and the other continued with MOPP given at two monthly intervals for 2 years. The complete response duration curve for maintained patients was always above that for unmaintained patients. 55% of patients receiving only 6 cycles were still in remission 2 years after treatment whereas 77% of patients treated for 2 years were in CR 2 years later. However, with follow up past 240 weeks, there is no statistically significant difference in survival of the complete responders. The explanation is that patients who relapsed after only 6 courses of MOPP had a 77% chance of achieving a second CR on retreatment with MOPP but in contrast all of those who relapsed after 15 cycles failed to be reinduced with

MOPP. This is a recurrent observation in the management of MOPP failures.

Their study also showed an excellent correlation between the sites of the largest masses of tumour before MOPP treatment and the site of initial recurrence, this being consistent with relapse of residual tumour rather than reinduction of disease.

With the improvement in the prognosis of patients with HD and the recognition of contiguous spread of disease it became necessary to develop staging procedures to identify accurately patients who might be cured by radiation alone thus avoiding the increase in morbidity associated with chemotherapy or combined modality treatment. The use of the Ann Arbor staging classification (Carbone et al, 1971)[37] including the use of laparotomy to pathologically stage patients in clinical trials over many years has revealed that even this is not enough and other prognostic indicators within any stage may also influence the outcome eg the bulk of mediastinal involvement in patients with Stage II disease is vital to determining whether or not the patient may be cured by radiation alone. Radiotherapy alone in patients with Stage IB and IIB disease has been reported to be followed by a 20% relapse rate, the majority in unirradiated sites (Goodman et al, 1977; Rosenberg et al, 1978)[77,145]. However, the British National Lymphoma Investigation

(BNLI) studies have reported that only 25% remain free of recurrence at 5 years (Haybittle et al, 1985)[85]. Hellman et al, 1978[86], attempted to increase relapse free survival by combining MOPP chemotherapy with radiotherapy in these patients. The alternative is to treat with MOPP at the time of relapse when half of these patients may be expected to remain disease free with two thirds surviving 3 years after induction of the second complete response (Weller et al, 1976)[185]. Initial treatment morbidity is less with this approach and approximately 90% of the total group may achieve extended disease free survival.

Patients relapsing after combination chemotherapy do not respond as well to further courses. Attempts have been made to produce non-cross-resistant chemotherapy regimes. Bonadonna et al, 1975[20], developed the regime ABVD (adriamycin, bleomycin, vinblastine and imidazole carboximide) which when used in previously untreated patients produced a CR rate of 75% which was equivalent to MOPP. When used in patients who have failed induction therapy the results with ABVD have been variable with a good overall response rate of 37-70% but with a CR rate of only 4-40%. Patients who are primary induction failures respond less well than patients who relapse after a CR no matter how short that remission lasted. However, even in studies showing a good response rate, remission duration is short and ABVD does not appear to be an effective curative regimen for patients with HD who

have failed MOPP (Case et al, 1977; Krikorian et al, 1978)[39,103]. It is because of this inability to produce significant long-term survival after MOPP failure and the failure of maintenance therapy to improve disease free survival, that efforts have been made to intensify the initial induction therapy. Non-cross-resistant combinations such as ABVD, have therefore been used either sequentially or in an alternating sequence with MOPP for induction therapy (Bonadonna et al, 1978)[21] and latterly these two regimes have been used in a hybrid form for induction (Klimo & Connors, 1985)[102] but at present numbers of patients are small and no clear survival advantage has yet been demonstrated.

Intensification of induction regimes means that patients who would have achieved a CR and long-term DFS on conventional chemotherapy with MOPP are being submitted to regimens with increased morbidity, therefore attempts to identify these patients and prevent unnecessary treatment of good prognosis patients has become increasingly important. One very poor prognosis group which has been identified by the BNLI study group is a very small subgroup of patients with lymphocyte depleted HD these patients appear to have only a 10% long term survival (BNLI study unpublished data) and would therefore be eligible for inclusion in a trial of intensive induction chemotherapy.

Patients with advanced HD are now treated mainly by MOPP combination chemotherapy or an equivalent regimen as primary treatment, up to 80% will achieve a CR, but approximately 30% of these patients will relapse (DeVita et al, 1980)[52]. Only a small proportion of the 20% of patients with primary MOPP resistance will achieve a CR with the use of an alternative non-cross-resistant regimen such as ABVD. Patients who relapse after MOPP chemotherapy may also achieve a second CR after ABVD or similar non-cross-resistant regimen but only 20-25% of these patients are likely to be disease free 3 years after finishing therapy (Santoro et al, 1982; Tannir et al, 1983)[151,167].

In an effort to improve the CR rates and reduce the relapse rates regimes which alternate non-cross-resistant regimens eg MOPP/ABVD from the start of treatment are now used by many centres. These have produced an improvement, as might be expected, but have resulted in less success with salvage regimens upon relapse (Santoro et al, 1984)[152]. One of the more successful salvage regimens following primary resistance to MOPP and ABVD or relapse after treatment with MOPP and ABVD whether given sequentially or alternately, is CEP (CCNU, Etoposide, Prednimustine). Bonadonna et al, 1985[22], reported a CR in 35% and a PR in a further 25%. Median duration of relapse free survival was 17 months and survival in CR >30 months.

It is because of the poor response rate and long-term DFS of conventional salvage regimens that we have employed intensive chemoradiotherapy regimes as salvage therapy using autologous bone marrow rescue to ameliorate the severe myelotoxicity thus produced in heavily pre-treated relapsed patients with HD.

It is in the context of primary resistance or relapse in these patients who have already received fairly intensive treatment, many of whom will also have had DXT, that intensive chemoradiotherapy with marrow rescue, whether allogeneic, syngeneic or autologous must be viewed.

PATIENTS

Fifteen patients with Hodgkin's disease, have been treated between August 1982 and August 1985 with this form of therapy. They were 13 males and 2 females. The median age was 29 years (range 13-55 years). 14 patients had received more than one chemotherapy regime and 11 had received anthracycline-containing combinations. 9 patients had also received radiotherapy. For the purposes of classification of disease at the time of grafting 'resistant relapse' (RR) indicates that the patient had progressive disease in spite of conventional chemotherapy whilst 'non resistant relapse' (NON RR) indicates that

the patient although relapsed was still responding to either second, third or fourth line therapy, or that the high dose chemoradiotherapy regime was employed as the second line regime at the time of relapse. Further details are given in Table 20.

## BONE MARROW HARVESTING, CRYOPRESERVATION AND REINFUSION

Bone marrow was harvested, cryopreserved and reinfused as previously described (Chapter 2; Linch et al, 1982)[107].

Bone marrow was harvested at relapse in 14 patients and at diagnosis in the remaining patient. The mean number of nucleated cells frozen per kg body weight was $1.62 \times 10^8$ cells/kg (range $0.7-3.3 \times 10^8$ cells/kg). The marrow was stored in liquid nitrogen for a median of 13 days (range 5-749 days) between harvesting and reinfusion of the first aliquot.

TABLE 20. PATIENT CHARACTERISTICS : HODGKIN'S DISEASE

| UPN | AGE | SEX | HIST @ DIAG | CLASS DIAG | DIAG ->ABMT | PREVIOUS TREATMENT | STATUS AT ABMT | ABMT CHEMO | STATUS POST ABMT | DFS | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 61 | 55 | M | NS | III | 52 | MOPP X 6<br>BACOP X 5 | RR | UCH I&II | CR | | DEAD 8 |
| 88 | 28 | M | NS | IIB | 47 | MOPP X 6<br>CCNU/Bl/<br>Vbl/P<br>DXT | RR | UCH I&II | CR | 5 | REL 36+ |
| 99 | 37 | M | NS | IA | 65 | LOPP<br>ABVD<br>DXT X 2 | RR | UCH I | NE | | DEAD day 14 |
| 113 | 46 | M | NS | IIIB | 15 | MOPP X 3<br>AVD X 5 | RR | UCH I | CR | 29+ | A & W |
| 116 | 24 | F | NS | IIAS | 22 | MOPP X 3<br>CCNU/Bl/Vbl<br>/P X 6 | RR | UCH I | CR | | DEAD day 40 |
| 146 | 25 | F | NS | IIA | 25 | LOPP X 6<br>EVAP X 7<br>DXT | RR | TBI 875 | PR | | DEAD 3 |
| 180 | 25 | M | NS | IIB | 25 | MOPP X 6<br>LOPP X 3<br>EVAP X 5<br>CCNU/Bl/Vind<br>DXT | RR | TBI 800 | PR | | DEAD 5 |
| 185 | 13 | M | MC | IVB | 15 | BACOP/<br>OPEC X 4 | NON RR | TBI/CYCLO | CR | 3 | REL 8 |
| 124 | 29 | M | ATYPICAL<br>/ IB | | 7 | CHOP X 1<br>HD ARA C X 1 | RR | BEAM | CR | | DEAD day 51 |
| 146 | 25 | F | NS | IIA | 25 | LOPP X 6<br>EVAP X 7<br>DXT | RR | TBI<br>875 | PR | | DEAD 3 |
| 155 | 30 | M | NS | IIA | 32 | BACOP/<br>OPEC X 3<br>DXT | RR | BEAM | CR | 17+ | A & W |
| 170 | 30 | M | NS | IIIB | 11 | LOPP X 3<br>CCNU/BLEO/<br>Vind X 9 | RR | BEAM | CR | | REL 14+ |
| 171 | 25 | M | NS | IIB | 40 | MOPP X 9<br>EVAP X 8<br>DXT | RR | BEAM | PR | | DEAD 7 |
| 177 | 36 | M | NS | IIIAS | 48 | LOPP X 3<br>MOPP X 4<br>LOPP/EVAP X 2<br>1/2 MOPP/EVAP<br>DXT | RR | BEAM | CR | 5 | REL 9 |
| 180 | 25 | M | NS | IIB | 25 | MOPP X 6<br>LOPP X 3<br>EVAP X 5<br>CCNU/Bl/Vind<br>DXT | RR | TBI<br>800 | PR | | DEAD 5 |
| 185 | 13 | M | MC<br>ATYPICAL | IVB | 15 | BACOP/<br>OPEC X 4 | NON RR | TBI/<br>CYCLO | CR | 3 | REL 8+ |
| 186 | 23 | M | NS | IIB | 20 | LOPP X 6<br>EVAP X 3<br>C/Vbl/Bl x 1<br>DXT X 2 | RR | BEAM | CR | 7+ | A & W |
| 188 | 30 | M | NS | IVB | 19 | LOPP X 9<br>DXT | NON RR | BEAM | CR | 7+ | A & W |

Legend for Table 20.

UPN = Unique patient number; HIST CLASS = Histological classification; NS = Nodular sclerosing; MC = Mixed cellularity; ST @ DIAG = Stage at diagnosis (This refers to the Ann Arbor staging classification); DIAG -> ABMT = The time interval between diagnosis and ABMT; PREVIOUS TREATMENT: CHOP = Cyclophosphamide, Adriamycin, Vincristine, Prednisolone; BACOP = Bleomycin, Adriamycin, Cyclophosphamide, Vincristine, Prednisolone; DXT = Radiotherapy; EVAP = VP16, Vinblastine, Adriamycin, Prednisolone; MOPP = Nitrogen Mustard, Vincristine, Procarbazine, Prednisolone; LOPP = Chlorambucil, Vincristine, Procarbazine, Prednisolone; CCNU/Bl/Vbl/P = Lomustine (CCNU), Bleomycin, Vinblastine, Prednisolone; ABVD = Adriamycin, Bleomycin, Vinblastine, Imidazole Carboximide; AVD = Adriamycin, Vinblastine, Imidazole Carboximide; HD ARA C = High dose Cytosine Arabinoside; OPEC = Vincristine, Prednisolone, VP16, Cyclophosphamide; CCNU/Bleo/Vind = Lomustine, Bleomycin, Vindesine; C/Vbl/Bl = Cyclophosphamide, Vinblastine, Bleomycin; STATUS AT ABMT: RR = Resistant Relapse; NON RR = Non Resistant Relapse; ABMT CHEMO = ABMT Chemotherapy; STATUS POST ABMT: CR = Complete Remission; PR = Partial Remission; NE = Not Evaluable; NR = No Response; DFS = Disease Free Survival; CURRENT STATUS: A & W = Alive and Well; REL = Relapse; All time intervals are given in months unless otherwise stated.

## TREATMENT PLAN

The treatment plan varied depending on the treatment regimen to be employed. If the UCH double protocol was employed then only one marrow harvest was performed and providing that more than $1.2x10^8$ nucleated cells/kg body weight were obtained post processing the harvested marrow was divided and half given after each course. If the harvested marrow contained $<1.2x10^8$ cells/kg then a second harvest was performed after recovery from ABMT I. UCH II was given as soon as there was haematological recovery from UCH I. Five patients received UCH I but only 2 received UCH I & II. UCH II was not given either because of septicaemic death following UCH I (UPN 99 & 116) or because having attained a CR after UCH I the patient declined UCH II (UPN 113).

The BEAM protocol was used as a single ABMT protocol.

## HIGH DOSE CHEMOTHERAPY REGIMENS

Two separate chemotherapy regimens were used; UCH I & II and BEAM. Three patients received total body irradiation (TBI) one with additional cyclophosphamide.

We decided to use the same regimen as for patients with NHL as the combination chemotherapy employed should

also produce a good response in patients with HD (Table 21). To avoid the use of more than one protocol in the unit we also adopted the BEAM protocol, for patients with HD, when we entered the collaborative protocol with the European centres for patients with NHL (Table 22).

Table 21. UCH I & II.

| UCH I | DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE | | * | * | * | | | | |
| 1.5 G / $M^2$ | | | | | | | | |
| BCNU | | * | | | | | | |
| 300 MG / $M^2$ | | | | | | | | |
| CYTOSINE ARABINOSIDE | | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | | |
| ABMT | | | | | | | * | |
| **UCH II** | | | | | | | | |
| METHOTREXATE | | * | | | | | | |
| 1.0 G / $M^2$ | | | | | | | | |
| BCNU | | * | | | | | | |
| 300 MG / $M^2$ | | | | | | | | |
| CYTOSINE ARABINOSIDE | | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | | |
| ABMT | | | | | | | * | |

Table 22. BEAM regimen.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| MELPHALAN | | | | | | * | |
| 140 MG / $M^2$ | | | | | | | |
| BCNU | * | | | | | | |
| 300 MG / $M^2$ | | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | |
| VPI6 | ** | ** | ** | ** | | | |
| 50 MG / $M^2$ | | | | | | | |
| ABMT | | | | | | | * |

In view of the sensitivity of HD to radiotherapy, occasional patients who had not had prior radiotherapy were treated with TBI. One patient received 10 grays TBI together with 60 mg/kg of cyclophosphamide on each of two consecutive days preceeding the radiotherapy. The other two patients who received TBI had 8 gray and 8.75 gray without additional chemotherapy.

# RESULTS

## Response To Therapy

Response to therapy was evaluated both clinically and by repeat computed axial tomography (CAT) scanning where previously abnormal. A complete remission was defined as the complete resolution of all signs and abnormal investigations in patients surviving beyond 30 days.

One patient with HD was non-evaluable because of a septicaemic death at day 14.

The remaining 14 patients all showed a response, 11 patients (79%) acheived a CR. In two of these patients marrow regeneration was delayed and these two patients died in aplasia at day 40 and 51 (UPN 116 and 124 respectively). Post mortem examination showed foci of necrosis without evidence of viable lymphoma. One patient (UPN 61) died in CR (8 months post ABMT) of acute cardiac failure of uncertain cause. Another 4 patients have relapsed, 3 are alive on further treatment 36, 13 and 8 months post ABMT, the fourth patient died in relapse 42 months post ABMT. Four patients remain alive and in CR 29, 17, 7, and 7 months post ABMT. Three patients only achieved a PR, they have since died with progressive disease 3, 5 and 7 months post ABMT (Figure 14).

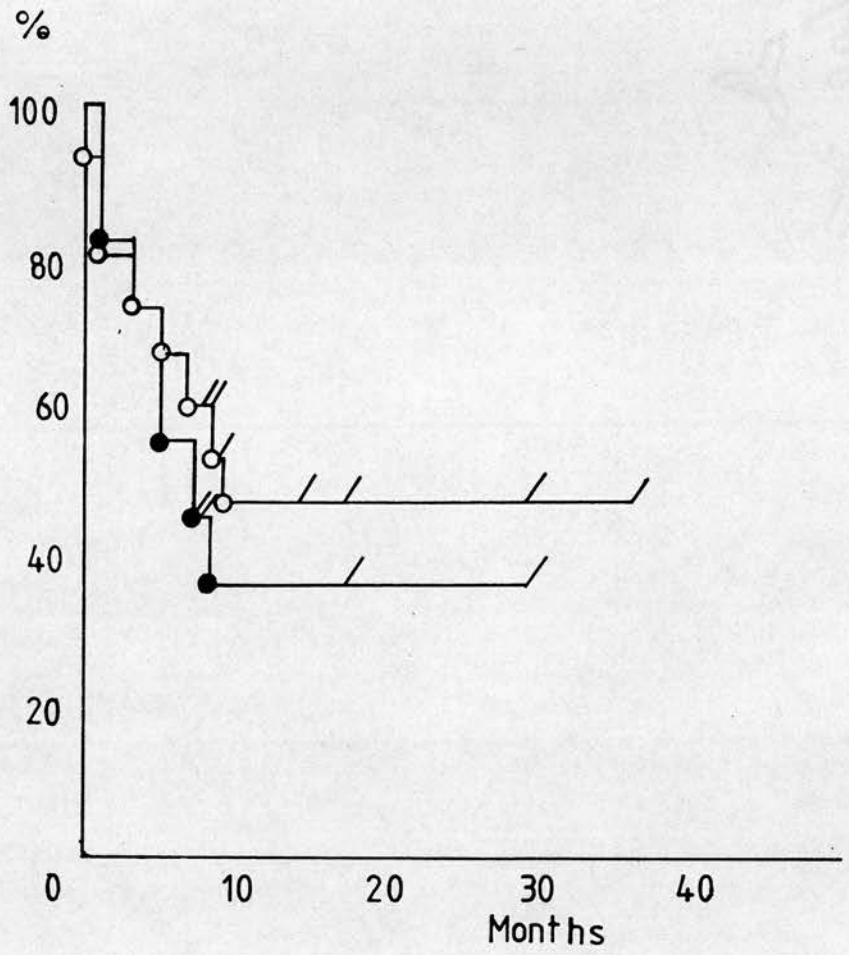



Figure 14. DFS in patients with HD who achieved a CR vs total survival of the group.

Patients who achieved a CR (n=11) ●——●

All patients (n=15) o——o

DISCUSSION

The Seattle group who pioneered the use of bone marrow transplantation in leukaemia, have treated 8 patients with MOPP-resistant disease (Appelbaum et al, 1985)[10], with high dose chemoradiotherapy followed by an allograft from an HLA identical sibling. 6 of these patients had received other chemotherapeutic agents as well as MOPP and 6 prior radiotherapy. All received TBI as part of the conditioning regimen, 7 cylophosphamide and one additional BCNU. 7 were thought to have achieved a CR. 5 died of complications, one patient relapsed at 4 months and has since died and 2 (25%) remain in unmaintained CR at 38 and 39 months. One of these survivors had transplantation as the first treatment for relapse after a MOPP induced CR of 6 months duration. This form of treatment demonstrates a very high response rate for MOPP-resistant disease and the authors suggest the long-term survival is comparable or better than most third line salvage regimens. However, in view of the high morbidity, it may not compare favourably with second line therapy for those who relapse after a long first CR (ie. >12 months).

Carella et al, 1985[38], reported the use of intensive chemotherapy with ABMT rescue in 13 patients with HD who either had primary resistance or who had relapsed after MOPP/ABVD given either sequentially or alternately, many

of whom had also received CEP and all of whom had had previous mantle DXT. 8 (61.5%) acheived a CR and 2 a PR. Much better response rates than any other conventional salvage regimen. 2 patients relapsed at 3 and 4 months, 6 (39%) remain in CR 2-34 months post ABMT on no treatment. In contrast to the allogeneic series reported from Seattle there was only one toxic death.

Canellos GP, 1985[35], has reviewed the use of BMT as salvage therapy for advanced HD (which includes the series of Carella et al, 1985)[38] in which he cites 49 patients treated with a variety of intensive regimens followed by ABMT. 25 (51%) achieved a CR, 10 (20%) of whom remain alive in CR (2-48 months) post ABMT. Only 3 of this 49 patients were treated with TBI, because of the high incidence of prior radiotherapy. One of the three achieved a CR and one died of interstitial pneumonitis. Most relapses occurred within 6 months.

Our early results in this study demonstrated similarly that in patients with disease resistant to conventional therapy, very high dose chemotherapy could still produce significant responses. This was particularly noticeable in the patients with relapsed resistant Hodgkin's Disease, in whom 9 of the 13 evaluable patients achieved a complete response. These responses were not in general sustained (Figure 14). We have therefore tried to use the very high dose chemoradiotherapy regimes earlier in the

course of the disease.

Of the eleven CR's in patients with HD 7 patients are alive but only 4 are still disease free 29, 17, 7 and 7 months post ABMT. 3 patients have died of procedural related complications whilst in CR, infection in two and cardiac failure in one. 4 patients have relapsed, 3 are still alive on chemotherapy 36, 14 and 7 months post ABMT, the other patient who relapsed died with progressive disease 9 months post ABMT.

The morbidity in this series has been high although not so high as following allograft (Appelbaum et al, 1985)[10]. To improve upon these results it will be necessary to proceed to ABMT at an earlier stage in the disease process when the patients are in better clinical condition and have less resistant disease. Most patients with HD can be cured by much safer initial therapy. It is therefore important to try and define patients with a poor prognosis. In the BNLI LOPP/MOPP study in HD, 3 situations have been identified in which early ABMT might be appropriate; i) no response to initial treatment; ii) PR or relapse from first line treatment if other poor prognostic features eg Grade II histology, Stage III or IV disease, a high ESR and B symptoms are also present; iii) all patients failing 2 modalities (either 2 chemotherapy regimens or chemotherapy and radiotherapy) as 5 year survival is only 20% (D Linch, 1986)[106].

In this and other studies of autologous bone marrow transplantation in lymphoma (Philip et al, 1983; Phillips et al, 1984)[128,130] the marrows were not infiltrated as determined by morphological criteria, but clearly the presence of occult disease cannot be excluded. However, in this study and that of Phillips et al, 1984[130], the main cause of failure was primary resistance to the high dose therapy used, and in those responding patients who relapsed, the relapses were mainly localized to a site of previous lymphomatous involvement.

This study thus shows that in patients with advanced relapsed HD, resistant to conventional dosage chemotherapy, very high dose chemoradiotherapy and ABMT may still produce a significant anti-tumour response. The morbidity and relapse rate have been high and future studies of very high dose chemotherapy must be directed at poor prognosis patients in an earlier stage of their disease.

# CHAPTER 7

## HAEMATOLOGICAL RECOVERY

### LARGE UNSTAINED CELLS (LUC'S)

It was observed during the course of this study that blood samples run on a Hemalog D90, often had a high percentage of LUC's in the period immediately prior to a detectable return of the WBC count. As this observation if confirmed might be relevant to clinical decisions as to whether or not to give the second half of a stored marrow (eg. in lymphoma patients in this study) or for allografted patients whether or not to reharvest the donor, we investigated this finding (Martin et al, 1986)[115].

An elevated percentage LUC count was detected following 105 transplant procedures. In only 2 cases was a rise in the percentage of LUC's not detected. Serial counts were available in 78 cases and in these cases the mean peak LUC count was 19.3% +/- (SE) with a range of 3.2-56.8%.

The relationship of the rise in total white cell count to the rise in percentage LUC's is shown for all 105

cases in which a rise occurred (Figure 15). In 72% of the 78 cases in which serial data was available, the rise in LUC's preceeded the rise in WBC by an average of 4 days. In 23 further cases in which the serial data is incomplete but evaluable in this respect, 20 also showed a rise in the percentage of LUC's predating the rise in WBC. In 17% the rise in LUC's and WBC were simultaneous and in only 8% of cases did the rise in WBC predate the rise in LUC percentage. The relationship between the rise in percentage LUC's and the rise in total WBC was similar for both the allografts and autografts (Table 23). The rise in percentage of LUC's predated the rise in WBC by an average of 4.0 days in patients with acute leukaemia, 3.0 days in patients with lymphoma, 4.1 days in patients with solid tumours and in the patients allografted was an average of 3.9 days.

Table 23. Relationship of rise in WBC to rise in the % of LUC's.

| TYPE OF BMT | | FOLLOWED | COINCIDED | PRECEEDED | NO RISE |
|---|---|---|---|---|---|
| ALLOGENEIC | 11 | 8 | 0 | 2 | 1 |
| AUTOLOGOUS | 67 | 48 | 13 | 5 | 1 |
| TOTALS | 78 | 56 | 13 | 7 | 2 |

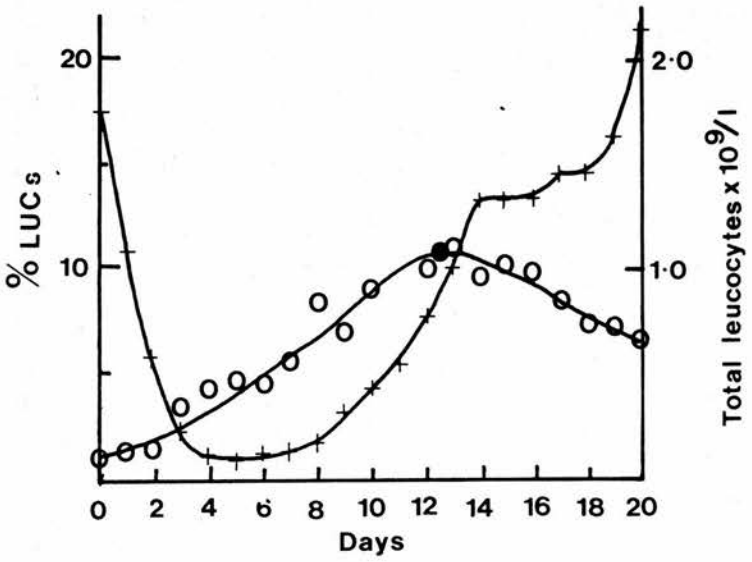



Figure 15. Appearance of total WBC and LUC's in the blood following allogeneic and autologous BMT.

\+ Total Leucocytes

O % LUC's

Values shown are means +/- SE following 94 transplant procedures.

Two patients showed regeneration of leucocytes without a rise in percentage of LUC's. One of these patients had ALL and was thought to have suffered from opportunistic lung infection. The other was a patient treated with a double cycle of high dose cyclophosphamide for small cell carcinoma of the lung. She suffered from a systemic candida infection in both cycles.

In only 2 cases in which a rise in the percentage of LUC's was noted was there failure of the WBC to rise. In one case this was due to death from an intra-cerebral haemorrhage on day 12 at a time when the percentage of LUC's was rising but the WBC had not risen above $0.3x10^9/L$. In the other case the percentage of LUC's rose to a peak of 22% on day 19 and then fell back to the normal range by 28 days. This patient developed an Aspergillus pneumonia during the regeneration period and died on day 33 without a leucocyte count ever rising above $0.3x10^9/L$.

The significance of these unusual patterns of LUC recovery is not clear.

Six patients received repeated granulocyte infusions for uncontrolled sepsis early after transplantation before evidence of regeneration. In no instance was there a rise in the percentage of LUC's detected.

Careful inspection of blood films with very high percentage LUC counts, during the early regeneration period, reveals that these cells are large mononuclear cells, often with indented nuclei showing some chromatin condensation but no nucleoli. They have moderate quantities of faintly basophilic cytoplasm which contains no obvious granules. These cells most commonly resemble monocytes, but LUC's are by definition non-specific esterase (NSE) and peroxidase negative. The NSE negativity has been confirmed by manual techniques. Furthermore, adherence for 1 hour to plastic, of ficoll hypaque separated mononuclear cells, did not reduce the percentage of LUC's as determined by re-analysis on the Hemalog D90 in two cases tested.

In four further cases, adherent cell depleted mononuclear cells containing more than 10% LUC were phenotyped with a range of monoclonal antibodies. The predominant cell type present was a CD8+ T cell (mean CD3% = 47%, mean CD8% = 42%). B cells as detected by anti-B1 represented only 3.5% of cells. There were no monocytic cells detected by staining with UCHM1 or Leu M3.

In one case over 20% of all leucocytes prior to separation were LUC's. Mononuclear cells from this

patient were analysed on a fluorescent activated cell sorter (FACS IV) and 34% of cells were found to be large cells distinct in size from a typical lymphocyte (Figure 16a). Analysis of the fluorescence profiles revealed that virtually all large cells were CD3+ CD8+ T cells (Figure 16b and 16c). Approximately half the large cells expressed HLA-DR antigens (Figure 16d). This CD3+ CD8+ phenotype of the large mononuclear cells in the early regenerative period was confirmed in 5 further cases by immuno-histological staining of blood smears.

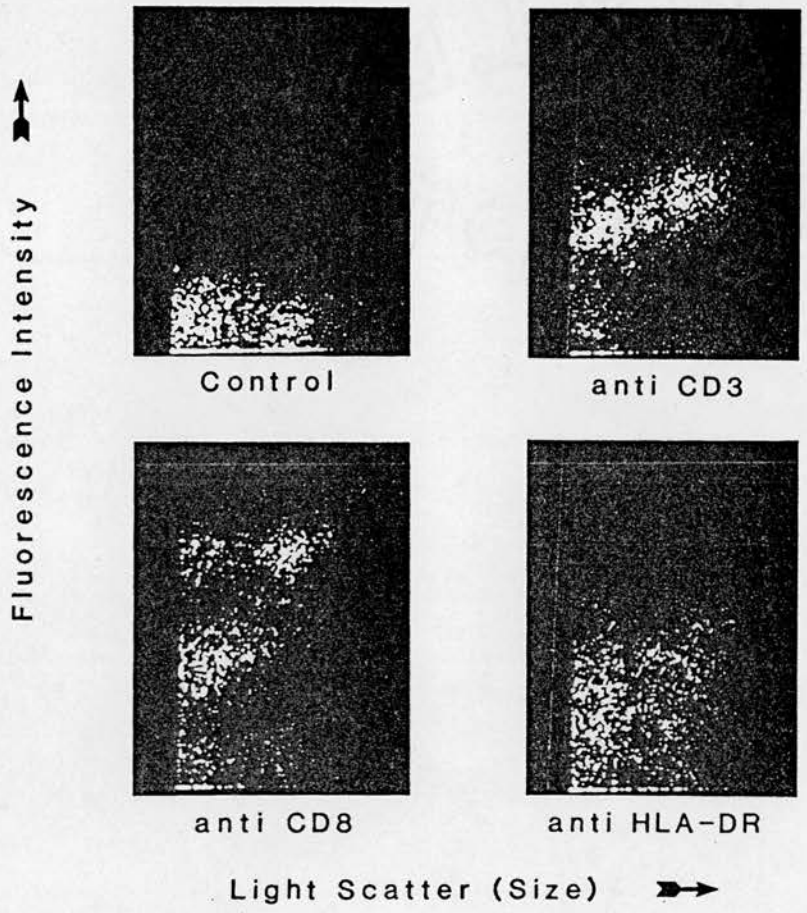



Figure 16a,b,c,d. Size and fluorescence profiles of peripheral blood mononuclear cells in the early stages of engraftment.

The time taken for haematological recovery until a total WBC count of $>1.0x10^9/L$, a neutrophil count of $>0.5x10^9/L$ and a platelet count of $>50x10^9/L$ is shown in Table 24.

All, except six patients, eventually achieved a platelet count of $>100x10^9/L$. Two of the six patients who failed to get full recovery died before evidence of regeneration, one regenerated with relapsed disease and 3 patients who were treated after first relapse, achieved a CR but their platelet counts were still $<100x10^9/L$ at the time they relapsed again.

The longer recovery time of patients with AML did not reach statistical significance, although delayed haematological recovery was the main reason for patients with AML failing to proceed to ABMT II.

Recovery of all parameters was statistically delayed after the second autograft (Table 25).

Assays of the GM CFC did not predict the speed of haematological recovery in this study (Table 26).

Table 24. The mean time in days for haematological recovery: Acute leukaemia (Day 0 = Day of marrow reinfusion).

ABMT I ONLY

| | AML+ALL | RANGE | |
|---|---|---|---|
| TOTAL WBC >1.0 X $10^9$/L | 19 | 11-40 | n = 42 * / ** |
| NEUTROPHILS >0.5 X $10^9$/L | 23 | 12-52 | |
| PLATELETS >50 X $10^9$/L | 36 | 13-228 | |

| | ALL | RANGE | AML | RANGE |
|---|---|---|---|---|
| | n = 18 ** | | n = 24 * | |
| TOTAL WBC >1.0 X $10^9$/L | 17 | 11-28 | 21 | 11-40 |
| NEUTROPHILS >0.5 X $10^9$/L | 20 | 12-42 | 26 | 16-52 |
| PLATELETS >50 X $10^9$/L | 25 | 13-71 | 44 | 17-228 |

There is no significant difference between AML and ALL.
$p > 0.05 < 0.1$

* One patient died day 12 before recovery and is not included

** A further patient's WBC is included but he died before platelet recovery

Table 25. Comparison of haematological recovery ABMT I VS II

AML ( n = 8 )

| | ABMT I | ABMT II | |
|---|---|---|---|
| TOTAL WBC >1.0 X $10^9$/L | 18 | 26 | p <0.05 |
| NEUTROPHILS >0.5 X $10^9$/L | 21 | 30 | NS |
| PLATELETS >50 X $10^9$/L | 27 | 42 | p <0.01 |

ALL ( n = 11 )

| | ABMT I | ABMT II | |
|---|---|---|---|
| TOTAL WBC >1.0 X $10^9$/L | 17 | 21 | p <0.01 |
| NEUTROPHILS >0.5 X $10^9$/L | 20 | 24 | p <0.05 |
| PLATELETS >50 X $10^9$/L | 22 | 35 | p <0.01 |

Table 26. Comparison of GM CFC with haematological recovery : ABMT I VS II*

| GM CFC | | TOTAL WBC >1 X $10^9$/L | | NEUTS >0.5 X $10^9$/L | | PLATELETS >50 X $10^9$/L | |
|---|---|---|---|---|---|---|---|
| I | II | I | II | I | II | I | II |
| GM CFC HIGHER IN ABMT I | | | | | | | |
| 1.09 | 0.87 | 13 | 25 | 17 | 32 | 28 | 51 |
| 1.66 | 1.28 | 12 | 13 | 20 | 17 | 17 | 26 |
| 3.49 | 1.69 | 17 | 31 | 18 | 36 | 35 | 36 |
| 6.23 | 0.94 | 21 | 33 | 21 | 33 | 21 | 47 |
| 6.32 | 3.89 | 13 | 18 | 14 | 18 | 20 | 34 |
| 6.9 | 3.09 | 20 | 26 | 31 | 28 | 33 | 45 |
| MEAN 4.28 | 1.96 | 16 | 24 | 20 | 27 | 26 | 40 |
| GM CFC HIGHER IN ABMT II | | | | | | | |
| 0.69 | 1.42 | 18 | 32+ | 19 | 32+ | 22 | 32+ |
| 3.06 | 3.6 | 20 | 25 | 27 | 25 | 26 | 28 |
| 4.49 | 6.44 | 14 | 17 | 20 | 28 | 20 | 35 |
| 9.66 | 10.46 | 28 | 24 | 39 | 35 | 39 | 49 |
| 13.62 | 15.04 | 19 | 26 | 21 | 26 | 33 | 45 |
| 12.54 | 15 | 14 | 16 | 16 | 14 | 20 | 26 |
| MEAN 7.34 | 8.66 | 19 | 23 | 24 | 27 | 27 | 38 |

* 12 patients who had adequate marrow aliquots stored to allow the assays to be run concurrently.

31 out of 36 patients survived beyond 30 days and were evaluable for haematological recovery. Two patients had not shown haematological recovery at the time of their deaths at days 40 and 51. In the 29 remaining patients the mean time from the day of ABMT to achieving a neutrophil count of $>0.5x10^9/L$ was 21 days (range 13-34 days) and a platelet count $>50x10^9/L$ was 26 days (range 12-43 days). Among these patients there was no relationship between the number of nucleated cells infused and the time to recovery of the neutrophil and platelet count.

In the two patients surviving beyond 30 days who did not regenerate the number of nucleated cells infused was $0.85x10^8$ cells/kg and $0.7x10^8$ cells/kg which was well below the mean of $1.67x10^8$ cells/kg (range $0.36-3.3x10^8$ cells/kg). These patients both had Hodgkin's disease and had been heavily pre-treated. With increasing numbers of patients there appears to be a more prolonged time to recovery in patients treated for HD although the mean nucleated cell count is similar: $1.62x10^8$ cells/kg and $1.64x10^8$ cells/kg in patients with HD and NHL respectively. Further details are given in Table 27.

All patients surviving the procedure achieved a platelet count of $>100x10^9/L$ except for one patient who

only achieved a PR and whose disease progessed before full recovery.

Table 27. The mean time in days for haematological recovery: Lymphoma (Day 0 = Day of marrow reinfusion).

| ABMT I ONLY | NHL* (n = 17) | RANGE | HD** (n = 12) | RANGE |
|---|---|---|---|---|
| TOTAL WBC >1.0 X $10^9$/L | 14 | 11-26 | 20 | 10-32 |
| NEUTROPHILS >0.5 X $10^9$/L | 19 | 13-29 | 25 | 13-34 |
| PLATELETS >50 X $10^9$/L | 23 | 14-38 | 29*** | 13-43 |

* Four patients died before recovery day 3, 5, 9 & 15, their results are not included

** Three patients died before recovery day 14, 40 & 51, their results are not included

*** Two further patient's WBC is included but both progressed and died before platelet recovery.

## DISCUSSION

An unexpected result of our study is the difference emerging between patients with AML and ALL in haematological recovery although in the small numbers in the study it fails to reach statistical significance. This difference has also been noted in the EBMTG study

(Gorin & Aegerter, 1986)[80]. A difference in our study was also noted in the rise in the percentage of LUC's in patients with ALL, with an apparent reduction in the rise, when compared to the results of patients with AML. If all the available LUC results for these two patient groups are compared, then patients with AML (n = 23 transplant procedures) showed an average rise in the percentage of LUC's to 22% (range 6.4-45.9%), four days before a demonstrable rise in the total WBC count, whilst patients with ALL (n = 14 transplant procedures) only showed an average rise to 15% (range none-29.2%), two days prior to a demonstrable rise in the total WBC count. These observations include both ABMT I & II results, but using a t test to compare the average rise in the percentage of LUC's $p<0.05$. If ABMT II results are excluded the average for the AML patient group is still significantly higher than that of the patients with ALL ($p<0.05$) (AML n = 16; ALL n = 8). The relevance of this observation is not clear.

The mean nucleated cell count was $1.9 \times 10^8$ cells/kg and $1.98 \times 10^8$ cells/kg in patients with AML and ALL respectively.

Assays of GM CFC have been reported (Spitzer et al, 1980)[162] to offer some predictive value in relation to numbers of stem cells present in the harvested bone marrow and the length of time to haematological recovery

post autografting. In those patients who have had a double ABMT, we have the unique opportunity of comparing results following 2 transplants in which the same conditioning regimen was given pre ABMT on each occasion to the same individual. There is no consistent difference between the number of GM CFC obtained in the first and second harvest (Table 26). In all except one patient the time to recovery of total WBC to $>1.0x10^9/L$ was prolonged after the second ABMT compared to the first and the time to recovery of platelets to $>50x10^9/L$, increased in all patients without exception. Neutrophil recovery to $>0.5x10^9/L$, was variable but separate analysis shows the changes did not coincide with the change in GM CFC.

A rise in the percentage of LUC's counted on the Hemalog D 90 appears indicative of successful engraftment following bone marrow transplantation. In 72% of cases this rise can be detected before the rise in total WBC count (ie. $>0.3x10^9/L$) can be reliably measured on the Coulter counter. In these cases the rise in percentage of LUC's is detected an average of 4 days before the leucocyte rise. In only one case, surviving long enough for evaluation, was a rise in the percentage of LUC's not followed by subsequent engraftment. This patient had developed a fungal pneumonia and it is likely that this caused toxic suppression of the graft after early engraftment had already commenced. Serial marrow biopsies were not performed and firm support for this hypothesis

that the percentage rise in LUC's predicted impending myeloid engraftment is lacking. This information is frequently of value to the clinician, particularly when engraftment is slow, the patient sick and reinfusion of further marrow is being considered. This applies to allografts and autografts in which only half the harvested marrow has been reinfused (lymphoma protocol in this study). It is in this context worthy of note that granulocyte transfusions did not cause a rise in the percentage of LUC's which might have been falsely interpreted as evidence of engraftment. The kinetics of early engraftment were similar in autografts and allografts regardless of the underlying disease, although the time to reach $0.5x10^9/L$ neutrophils in the peripheral blood was delayed in patients with acute leukaemia receiving autografts (24.3 days in patients autografted for acute leukaemia compared to 11.4 days in the remainder).

The LUC's, although of monocytoid appearance, are shown to be T lymphocytes of the CD8+ subset (See earlier this Chapter). It has previously been reported that CD8+ lymphocytes predominate in the peripheral blood after both autologous and allogeneic marrow transplants (Linch et al, 1983)[108] and it is now apparent that in the majority of cases this type of lymphocyte is among the first to appear in the blood. It is possible that this initial T cell expansion may facilitate myeloid

engraftment. There is some evidence that extensive T cell depletion of donor marrow for the prevention of GVHD may lead to delayed engraftment and even graft failure in some cases (Waldmann et al, 1984)[180].

The delay in haematological recovery following ABMT I in patients with AML has been the major reason for our deferring patients who would otherwise have been eligible to proceed to ABMT II (Table 5, Chapter 3). This has resulted in only eight patients (33%) with AML receiving both ABMT I & II, whilst eleven (61%) of patients with ALL have received both ABMT I & II. Although the delay has failed to reach a statistical significance when compared to the recovery of patients with ALL, we regard this as the major toxicity of our double ABMT approach to the treatment of patients with AML in first remission. The prolonged thrombocytopenia which may follow (Goldstone et al, 1986)[74] has been particularly worrying and has been associated with haemorrhagic complications including two deaths after WBC recovery, both from a cerebral haemorrhage (patient details not included in this study).

We have studied some of these patients for auto-antibodies but have not demonstrated any platelet auto-antibodies. Bone marrow aspirates and trephines suggest a reduction in cellularity is more likely to be responsible for the slow recovery seen in some patients.

The haematological recovery following ABMT in patients with NHL and HD is similar to that occurring after ABMT in patients with leukaemia. There is a tendency for patients with HD to take longer to regenerate than patients treated for NHL but this does not reach statistical significance. The nucleated cell count returned in each group was similar; $1.64x10^8$ cells/kg in patients with NHL and $1.62x10^8$ cells/kg in patients with HD. The longer regeneration in patients with HD may reflect their heavier prior treatment when compared to the patients with NHL.

There has been no failure to graft in either the patients treated for leukaemia or NHL, but there have been two patients with HD who have died in aplasia day 40 and 51. One patient (UPN 116) was treated with UCH I and the other (UPN 124) with BEAM. They both received nucleated cell counts in the lower range; 0.7 and $0.85x10^8$ cells/kg. It is therefore possible that this contributed to both their deaths. This is the reason we now recommend a minimum of $1.0x10^8$ cells/kg body weight should be stored before the patient proceeds to autograft. Interestingly, AH Goldstone, 1986[74], reporting the collective EBMTG study results, found that the nucleated cell count was the only factor analysed which correlated with overall survival in patients with HD, post ABMT. This was no longer significant if patients who died procedure related deaths were excluded, suggesting

low cell yields at marrow harvest in these patients may be a significant problem associated with the use of ABMT in patients with HD, and may contribute significantly to an increase in morbidity.

If high dose chemoradiotherapy is to be successful in Hodgkin's disease, it will need to be used earlier in the course of the disease, when the marrow is more likely to be cellular, thus avoiding low cell yields at marrow harvest together with the associated increase in morbidity.

# CHAPTER 8

# MORBIDITY

## ACUTE LEUKAEMIA

### SUPPORT REQUIREMENTS

Patients remained as in-patients at University College Hospital for an average of 37 days, during treatment and recovery post ABMT. In spite of the greater delay in haematological recovery post ABMT for AML, the time in hospital was similar for both groups: 34 days for ALL compared to 36 days for AML. The 5 patients treated in relapse stayed an average of 44 days, which probably reflects their poorer physical condition at the time of treatment. The average in-patient stay during ABMT I and II for those who had both (17 patients), was 31 and 41 days respectively.

Blood product support was similar in both AML and ALL, with a greater amount being required for patients undergoing ABMT II. There were too few patients treated as reinduction to note a significant difference. The number of units of blood required to support patients

undergoing ABMT I & II was 8 and 12 units respectively, and the number of units of platelets required 74 and 93.

Delay in haematological recovery was the main reason for not proceeding to ABMT II. As might be expected, the number of units of blood and platelets required during ABMT I by those patients who proceeded to ABMT II were less than the number of units required by those who had ABMT I only. Patients who had ABMT I & II required on average 7 units of blood and 56 units of platelets each during ABMT I, whilst those who had only ABMT I required 9 units of blood and 92 units of platelets each.

In 9 out of 50 procedures (18%), normal donor granulocytes were collected and given because of severe sepsis. In the same number other blood products were required, eg. FFP during bleeding episodes. There was no difference between AML and ALL, or between ABMT I and II.

Blood products were not irradiated prior to reinfusion but no patient in this series developed evidence of clinically recognisable GVHD.

All except 3 patients became pyrexial with their temperature rising to >38 $^{O}$C during either ABMT I or II. The average number of days patients had a temperature >38.0$^{0}$C during ABMT I and during ABMT II was 9 and 8 days respectively.

The average number of antibiotics used in each patient to treat pyrexial/infective episodes was five (this included acyclovir, metronidazole and intravenous amphotericin) in all groups. Only one patient required no antibiotic therapy during ABMT I.

Weight loss was a common problem, averaging 5.7 kg in patients with both AML and ALL; parenteral nutrition was employed in six patients, five patients with ALL and one patient with AML.

## EARLY COMPLICATIONS

### INFECTIVE COMPLICATIONS

5 patients died during the procedure; 2 during ABMT I and 3 during ABMT II. Four were thought clinically to be infective deaths as there was rapidly progressive pulmonary shadowing and fever, with death occurring at days 23, 25, 28 and 32. All four patients had ALL. One was proven due to aspergillus fumigatus. The other three had no organism isolated. Post mortem changes were consistent with the adult respiratory distress syndrome but were not specific for any infective organism, drug toxicity cannot therefore be excluded.

One patient developed an aspergilloma during ABMT II from which she eventually recovered (UPN 69) another patient developed a candida septicaemia from which she also recovered (UPN 51), both these were also patients with ALL. No patient with AML developed a proven systemic fungal or yeast infection or died an infective death.

By contrast, Gram negative infections appeared more common in the patients with AML than in the patients with ALL (Table 28). There were ten episodes of gram negative septicaemia in the 32 autograft procedures (31%) performed in patients with AML and only three episodes in the 29 procedures (10%) performed in patients with ALL. A further three patients with AML developed an ecthyma gangrenosum with pseudomonas isolated. Only one patient with ALL developed an abscess from which pseudomonas was isolated. This difference in the incidence of severe gram negative infections is statistically significant ($X^2=5.2$, $p<0.05$). Gram positive septicaemias were more common in patients with ALL (41%) than AML (22%), but this difference did not reach statistical significance.

Further details of the infections and significant microbiological isolates can be found in Table 28 & 29.

Table 28. Comparison of septicaemic episodes: AML vs ALL, and associated lesions.

| | AML (n = 24) | ALL (n = 18) |
|---|---|---|
| BACTERAEMIA/SEPTICAEMIA | | |
| GRAM -VE * | 10 | 3 |
| GRAM +VE ** | 7 | 12 |
| CANDIDA | 0 | 2 |
| 2 OR MORE ORGANISMS. | 4/12 | 6/9 |
| SAME ORGANISM ABNT I&II | 1/12 | |
| ECTHYMA GANGRENOSUM | 3 | 0 |
| Pseudomonas aeruginosa isolated | | |
| ABSCESS (Not Septicaemic) | 0 | 1 |
| Pseudomonas aeruginosa isolated | | |

* Pseudomonas aeruginosa 4, Escherichia coli 5, Klebsiella aerogenes 2, Flavobacterium species 1, 1 unidentified organism of doubtful significance.

** Coagulase -ve staphylococci 7, Streptococcus sanguis 3, Streptococcus mitis 2, a haemolytic streptococcus 1, B haemolytic streptoccocus 1, Staphylococcus aureus 1, Streptococcus mitior 1, Streptococcus faecalis 1, Streptococcus milleri 1, Clostridium sporogenes 1.
6 were of doubtful significance.

Table 29. Comparison of other positive microbiological isolates: AML vs ALL

| | AML (n = 24) | ALL (n = 18) |
|---|---|---|
| +VE CNDIDA SPECIES ISOLATES | | |
| 1 OR MORE SITES | 14 | 11 |
| ISOLATES FROM HICKMAN ENTRY SITES | | |
| Coagulase -ve staphylococci | 21 | 15 |
| Diptheroids | 11 | 4 |
| Staphylococcus aureus | 3 | 2 |
| OTHERS: | 0 | 3 |
| (Streptococcus faecalis, Bacillus brevis, Pseudomonas aeruginosa) | | |
| OTHER SIGNIFICANT ISOLATES | | |
| URINE | 2 | 4 |
| SPUTUM | 1 | 3 |
| | | (2 aspergillus fumigatus) |
| FAECES: | | |
| Clostridium difficile | 4 | 4 |
| Toxin only | 3 | 1 |

NON-INFECTIVE COMPLICATIONS

Cytotoxic induced nausea and vomiting occurred in all patients but was not usually severe.

Haemorrhagic

Haemorrhagic cystitis occurred in only two patients, one patient with AML and one with ALL. This was in spite of the use of 600 mg of mesna / 1 gm of cyclophosphamide. After this all patients received 1 gm of mesna / 1 gm of cyclophosphamide.

One early death (UPN 92) was from an intra-cerebral haemorrhage day 12, before regeneration. One patient (UPN 103) had mild but continuous bleeding per-vaginum throughout ABMT I, even though she was treated with norethisterone. The bleeding resolved spontaneously when her platelet count rose. Two patients (UPN 55 & 125) had significant gastro-intestinal haemorrhage consuming large amounts of platelets (ie. >200 units of platelets each), resolution occurred upon autologous platelet recovery without identification of a specific lesion. Except for the one patient with ALL who developed haemorrhagic cystitis post cyclophosphamide, all patients who experienced noticeable haemorrhagic complications were patients with AML.

Cardiac Toxicity

One patient (UPN 174) with ALL developed pericarditis post the chemotherapy of ABMT I and did not continue to ABMT II because of this. One patient (UPN B4) with AML developed left ventricular failure day -4, presumed due to the cyclophosphamide and the final days dose of this drug was therefore omitted. Delayed haematological recovery prevented ABMT II in this patient who relapsed day 191 and has since died.

Other

One patient (UPN 143) with AML and with no past history of epilepsy had a grand mal convulsion, for which there was no obvious explanation, day 98 (day 24 post ABMT II) when the platelet count was $36x10^9/L$, unsupported, and the total WBC and neutrophil count were 2.6 and $1.1x10^9/L$ respectively. When the anticonvulsants were withdrawn 1 month later he suffered a further fit and has had to remain on medication.

## INFECTIVE COMPLICATIONS

One patient (UPN 51) with ALL developed a Listeria septicaemia nearly 2 years post ABMT.

Two patients (UPN 67 & 69) both with ALL suffered Herpes zoster infections treated with intravenous acyclovir, one occurring within the first month after discharge and the other at the end of the first year.

All the above patients had ALL and were therefore on maintenance chemotherapy at the time of their infections.

Patients with AML received no maintenance chemotherapy and the only patient with AML (UPN 108) to experience infective problems post ABMT, had a Herpes simplex lesion on her lip treated with oral Acyclovir 4 months post ABMT.

A further patient with AML (UPN 161) developed a transient thrombocytopenia which resolved without treatment and may have been due to an intercurrent viral infection, as has previously been reported following allografts (Deeg et al, 1984 : First et al, 1985)[46,65] although no infection was demonstrated.

NON-INFECTIVE COMPLICATIONS

Pulmonary: One patient with ALL (UPN 69) was treated with several months of intravenous amphotericin for a pulmonary aspergilloma post ABMT II. She was noted to have a severe restrictive ventilatory defect with a very reduced TCO more than 2 years after ABMT. Before this could be further investigated, she suffered an extra-medullary relapse which presented as a breast lump, biopsy proving it to be sheets of lymphoblasts. Extramedullary relapse presenting as a breast lump appears to have been reported only once before (Ellegaard et al 1984)[58]. She received further chemotherapy but suffered a medullary relapse and died 36 months post ABMT. Her last admission was complicated by a spontaneous pneumothorax but the nature of her underlying pulmonary problem was never resolved.

Fertility: Gonadal failure post TBI is almost universal. However, in patients treated with high dose cyclophosphamide only, before marrow transplantation for aplastic anaemia, two thirds of adult male patients have a return of gonadal function with normal gonadotrophin levels and low to normal sperm counts. In women the result appears dependent on age : if <26 years at the time of treatment the secondary amennorrhoea lasts for a median of 6 months and gonadotrophin levels are normal, if treated when >26 years old then ovarian failure with an early menopause is

the rule (Deeg et al, 1984)[46].

We have not routinely measured gonadotrophin levels in our patients.

One male patient (UPN 19), was 24 years old when treated for AML with the double ABMT protocol. He requested fertility investigations 18 months post ABMT. He has a normal sperm count and is potentially fertile but he has a raised gonadotrophin level suggesting testicular damage.

Two female patients with AML (UPN 108 & 128) were treated at 39 and 32 years of age respectively. The older has remained amenorrhoeic since her double ABMT over 2 years ago and is presumed to have ovarian failure, the other continues to have erratic menstruation. She has been reviewed by the gynaecologists but has not been investigated for infertility.

Other: One patient with ALL (UPN 51) has developed a cataract 2 years post ABMT. This may be the result of the chemotherapy regimen used for ABMT but could also be caused by steroid therapy as she has ALL and has received significant amounts of steroids since her diagnosis in 1977.

DISCUSSION

An unexpected result of our study is the difference emerging between patients with AML and ALL in the incidence and morbidity of the various infections and thus in overall survival.

One patient with ALL treated in first remission developed an aspergilloma; two further serious fungal infections occurred in the ten patients with ALL treated at a later stage of their disease, one a fatal aspergillus pneumonia and the other a candida septicaemia from which the patient recovered. Systemic fungal infection caused by Aspergillus and Candida species are generally associated with defects in neutrophil function or total low neutrophil counts. The ABMT protocol was identical in the two groups and patients with AML were generally neutropenic for longer periods, but there were no systemic fungal infections documented in patients with AML. The patients treatment prior to ABMT may be the important difference, with the craniospinal prophylaxis or the steroids which all patients with ALL receive, being a possible cause.

LUC results available for patients with ALL (n=14) showed an average rise in the percentage of LUC's to 15% (range none-29.2%), two days prior to a demonstrable rise in the total WBC count compared to an average rise of 22%

(range 6.4-45.9%), four days before a rise in the total WBC count in patients with AML (n=23). The average rise in the percentage of LUC's in patients with AML is significantly higher ($p<0.05$) when compared to patients with ALL (Chapter 7). We have demonstrated these LUC's to be T lymphocytes. This raises the possibility that T lymphocyte recovery may be impaired in patients with ALL, putting them at greater risk of fungal infection when compared to patients with AML.

de Gast et al, 1985[48], have suggested that T cell proliferation after ABMT is mainly due to proliferation of mature T cells in the graft, not regeneration from stem cells. This might explain the normal pattern of rise in the percentage of LUC's in the two patients who died of aspergillus infection, although they never showed any evidence of engraftment, if mature T cells remain unaffected whilst stem cells are inhibited. Aspergillus infection in patients not undergoing transplantation has been demonstrated to be associated with clinical anaemia and 'in vivo' studies have demonstrated inhibition of erythroid colony formation, probably by a soluble factor (Zanjani et al, 1982)[190]. If this same inhibition could be demonstrated for granulocyte colonies it might explain the failure of both our patients who died of aspergillus pneumonia to engraft.

The higher incidence of severe gram -ve infections

which is statistically significant ($X^2$=5.2, p<0.05), in patients with AML compared to patients with ALL does not appear to have been reported from other series. Enhanced susceptibility to infection with these bacteria is caused by neutropenia and defects in cell-mediated immunity. The greater period of neutropenia following ABMT in patients autografted for AML may be responsible for the increase in the incidence of these infections compared to patients autografted for ALL.

Immune reconstitution has been demonstrated to be disordered for prolonged periods post ABMT (Linch et al, 1983)[108], however, in this series no serious infective episodes have occurred in patients who were not on maintenance chemotherapy.

Fertility investigations of future patients will establish whether this double protocol results in sterility or not. If it does not result in universal infertility, which is the rule after an allograft with cyclophosphamide and TBI conditioning, then this would be an advantage of high dose chemotherapy and ABMT regimens which do not employ TBI, in young patients.

## COMPLICATIONS

### INFECTIVE COMPLICATIONS

Five patients (14%) died of sepsis before engraftment.

Septicaemia: Four of the patients who died had clinical septicaemia. The organisms isolated varied (Table 30). One patient had multiple isolates in the week before his death including a coagulase negative staphylococcus which was isolated on 5 occasions.

Table 30. Organisms isolated from the blood in patients dying of septicaemia.

| UNIQUE PATIENT NUMBER | |
|---|---|
| 75 | No Positive isolate |
| 99 | Acinetobacter species |
| 116 | Staphylococcus aureus |
| 161 | {Staphylococcus aureus |
| | {Streptococcus pneumoniae |
| | {Bacillus species |
| | {Coagulase -ve staphylococcus* |

* Isolated 5 times in the week before death.

Organisms were isolated from the blood in 15 patients (50%) with many having more than one positive isolate

Table 31. Positive microbiological isolates from the blood.

| | |
|---|---|
| Gram negative: | |
| Acinetobacter species | 3 |
| Klebsiella aerogenes | 1 |
| Escherischia coli | 1 |
| TOTAL | 5 |
| Gram positive: | |
| Coagulase -ve staphylococcus | 9 |
| Staphylococcus aureus | 2 |
| Streptococcus pneumoniae | 1 |
| Streptococcus faecalis | 1 |
| Streptococcus viridans | 1 |
| B haemolytic streptococcus | 1 |
| Gp B streptococcus | 1 |
| TOTAL | 16 |

Although there was a large number of positive isolates of coagulase negative staphylococci, these organisms were almost universally isolated from skin sites and it is not clear how many of the positive blood isolates represent sepsis rather than contamination.

Fungal Infections:

The cause of death in one of the patients who died before regeneration was a fungal pneumonia, due to Aspergillus fumigatus.

Candida was isolated from multiple sites in 22 patients (73%) in spite of anti-fungal prophylaxis but no systemic candida infection was identified.

Other: There were other non-fatal infections with pyrexias occurring in 30 of the remaining 31 patients. One patient had a pneumococcal pneumonia.

9 patients had urinary tract infections, 7 Gm -ve. Infection necessitated removal of the Hickman catheter in 5 patients, 3 because of associated septicaemia with a coagulase negative staphylococcus and 2 because of severe infection at the exit site.

NON-INFECTIVE COMPLICATIONS

Immediate: Two patients (UPN 166 & 168) died at day 3 and 5, one was presumed due to tumour infiltration of the myocardium and the other to tracheal obstruction by tumour, neither patient had a post mortem and it is possible that both deaths were contributed to by drug toxicity.

Cardiotoxicity: One patient (UPN 61) died a cardiac death 8 months post ABMT whilst in CR. This patient had HD and

his death may reflect cumulative toxicity from drugs and irradiation.

Other drug related toxicity: One patient (UPN 88) suffered haemorrhagic cystitis, in spite of adequate hydration and mesnum administration. One patient (UPN 181) suffered a severe generalised skin rash which appeared likely to be due to one of the drugs (the chemotherapy protocol used in this patient was BEAM).

Other: One patient (UPN 34) had his Hickman catheter removed because of a subclavian vein thrombosis.

## DISCUSSION

The morbidity in this series has been high with sepsis the major complication and procedural related deaths occurring in 8 of the 36 patients (22%). This is perhaps not surprising in view of the poor clinical condition of many of these patients with either end stage or relapsed disease. Similarly high numbers of treatment related deaths have been reported in two other series of high dose therapy and ABMT in patients with lymphoma who had received extensive previous therapy (Philip et al, 1983; Phillips et al, 1984)[128,130].

Our current aim is to employ this treatment earlier in

the course of the disease. It is hoped that by transplanting patients early they will be in a better clinical condition and there will be less morbidity, as in our group of patients with AML treated in CR1.

The lymphoma patients had all received steroids and many of them had also received radiotherapy prior to being treated with the intensive chemoradiotherapy regimens followed by ABMT employed here. Systemic fungal infections have occurred in the patients treated with ABMT for lymphoma as they have in the patients treated for ALL. In this present series, the poor clinical condition of many of the lymphoma patients when treated with the pre-ABMT conditioning regimen may have contributed to their susceptibility to these infections. The inclusion of patients who are clinically fitter in the future, may make it possible to ascertain whether the incidence of systemic fungal infections is related to the previous steroid therapy, previous irradiation or perhaps both.

# CHAPTER 9

## CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE PROTOCOLS

The results of this study demonstrate the feasibility of using intensive chemoradiotherapy regimens with autologous marrow rescue in the treatment of patients with acute leukaemia in remission or relapse and patients with relapsed heavily pre-treated Hodgkin's disease and non-Hodgkin's lymphoma. The number of patients treated is still small and follow up still relatively short.

The following are my suggestions for regimens to treat each of these diseases in the light of the experience gained in this study and a review of other currently reported regimens.

### ACUTE MYELOID LEUKAEMIA

#### FIRST REMISSION PATIENTS

The most important pre-requisite for long term DFS and possible cure is to acheive a CR. Once a CR has been induced some form of intensive consolidation must be

given in an attempt to achieve long-term DFS.

At presentation patients should be induced on one of the more intensive induction regimes now available (eg daunorubicin 50 $mg/m^2$ x 3, cytosine arabinoside and thioguanine both 200 $mg/m^2$ daily for 10 days, this is one arm of the MRC AML IX protocol)[120]. As soon as possible after achieving a CR the patients should be treated by some form of intensive consolidation therapy.

The risk of leukaemic relapse post allogeneic marrow transplantation is approximately 15% and is not affected by the age of the patient.

Patients who have an HLA identical sibling donor should therefore be considered for an allograft. However, because of the impact of non-leukaemic deaths, the chance of being alive at 2 years is approximately 70% for patients <20 years of age, 50% for patients 20-29 years old and 40% for patients 30-50 years of age (Thomas et al, 1982)[174].

In our series of 16 patients with AML treated with high dose chemotherapy (Table 32) followed by ABMT in CR1 there have been no non-leukaemic deaths, 13/16 were >30 years of age (the oldest was 55 years, UPN B4). Their actuarial survival in unmaintained remission at 2 years is 62%. (No further relapses have occurred in this group

last date of follow-up 30.9.86).

Table 32. High dose chemotherapy regimen for patients with acute leukaemia ABMT I & II.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE 1.5 G / $M^2$ | * | * | * | | | |
| BCNU 300 MG / $M^2$ | * | | | | | |
| CYTOSINE ARABINOSIDE 100 MG / $M^2$ | ** | ** | ** | ** | | |
| THIOGUANINE 100 MG / $M^2$ | ** | ** | ** | ** | | |
| ADRIAMYCIN 50 MG / $M^2$ | * | | | | | |
| ABMT | | | | | | * |

I would therefore propose that as the risk of relapse is higher post ABMT, as demonstrated by our series (Chapter 3; AML), patients <20 years of age with an HLA identical sibling should be allografted.

Patients >30 years of age should be treated by our existing ABMT protocol, as the higher relapse rate is

counter balanced by the absence of non-leukaemic deaths resulting in much better long-term survival.

There are only two patients in our series between 20-29 years (UPN 19 & 148) and both are alive and in CR1, 2 and 5 years post ABMT. Assuming the same relapse rate then this age group should still have a survival advantage when treated with our ABMT protocol compared to allografting. I would therefore recommend ABMT in this age group also.

The importance of the double protocol is difficult to assess. No relapse has occurred in patients completing ABMT I & II. If completion of the double protocol is important to prevent relapse, with 60% relapse occurring after a single ABMT. Then our ABMT protocol for patients completing only ABMT I has no advantage to allografting in any age group.

All the patients who have relapsed took longer than two months to achieve CR1 and this may account in part for their slower haematological recovery, preventing the implementation of ABMT II, as they had received more treatment pre-ABMT. I would propose that any patient who takes longer than two months to acheive CR1 should have two harvests before ABMT I. An alternative would be to halve the first harvest as has been done in some of our lymphoma patients but halving a marrow in this group who

were slow to regenerate anyway, may further prolong their period of aplasia and significantly increase morbidity and possibly mortality. Once these patients had recovered physically from ABMT I, they could progress to ABMT II, any delay in haematological recovery post ABMT I could be ignored unless very severe as there is no need for a second harvest post ABMT I (Figure 17 & 18).

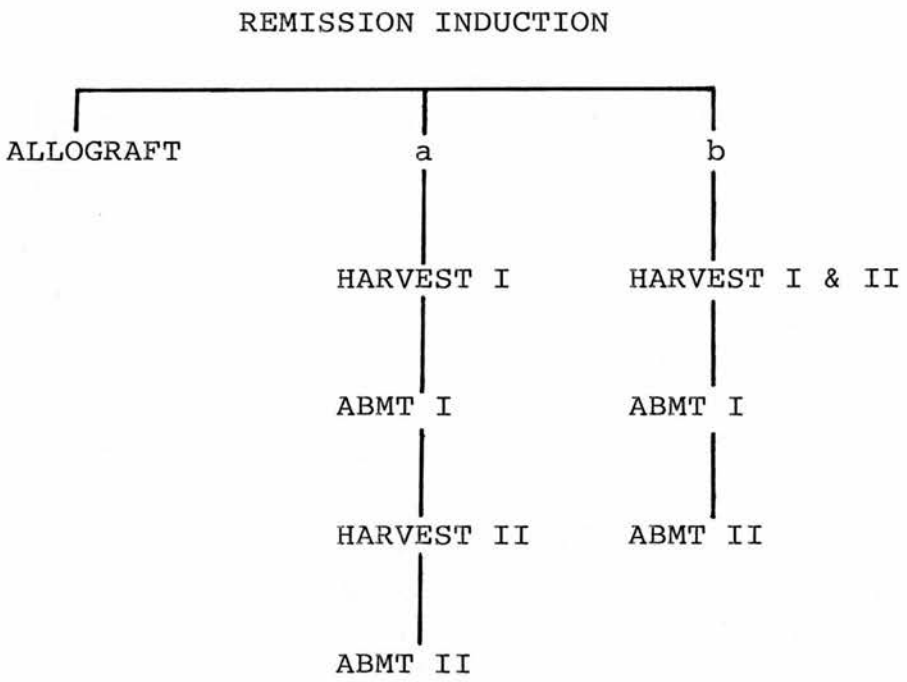



Figure 17. Plan for treating patients with AML in first remission who are <20 years old, a) patients who acheive CR1 in <2/12, b) patients who take >2/12 (see text for further explanation and drug regimens).

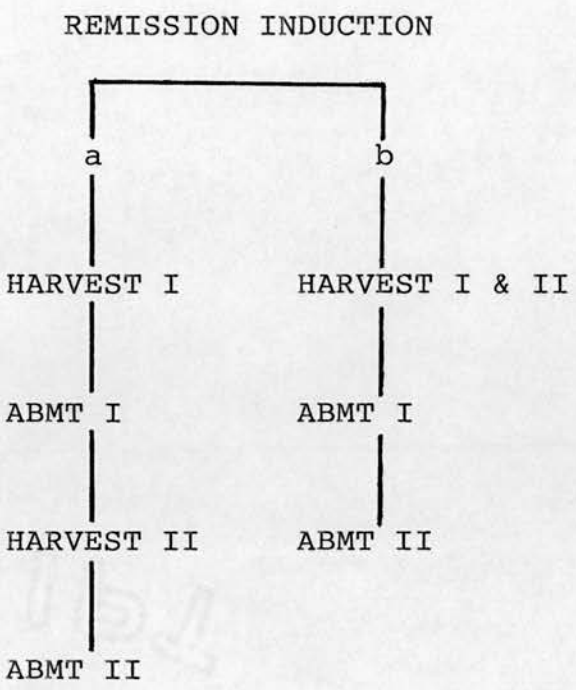



Figure 18. Plan for treating patients with AML in first remission who are >20 years old, a) patients who acheive CR1 in <2/12, b) patients who take >2/12 (see text for further explanation and drug regimens).

If the time to achieve CR1 continues to prove a good predictor of relapse following our ABMT protocol, irrespective of whether or not the patient receives ABMT I or ABMT I & II, then patients who take longer than 2 months to reach CR1 would have a very high likelihood of relapse following ABMT and should be allografted if they have a suitable donor.

It is possible that the predictive value of this time interval is partly because it indicates those patients

most likely to be able to tolerate 2 grafts - only one patient in our series who took more than 2/12 to achieve CR1 has so far tolerated the second autograft.

There is at present no relapse in the patients who complete both ABMT I & II on this protocol, but 60% of those who received only ABMT I have already relapsed.

A separate study to investigate the best time to reharvest patients post ABMT would be useful. It may be possible to identify a time post ABMT at which a higher yield of stem cells may be obtained, as has been reported to occur in the peripheral blood post conventional dosage chemotherapy (Richman et al, 1976)[140]. It may be useful to consider boosting the harvest with stem cells collected from the peripheral blood.

Patients who refuse BMT should be treated with the most intensive chemotherapy regimen possible eg. VAPA (Weinstein et al, 1983)[184], MRC AML9[120].

Data is at present very limited but there is some evidence that patients treated with a consolidation regimen containing different drugs to the initial induction regimen have better DFS (Bloomfield CD, 1985; Wolff et al, 1985)[18,187]. This would be in keeping with the accumulating evidence in favour of this approach in patients with advanced Hodgkin's disease and ALL (Skipper

et al, 1964; Goldie et al 1982)[160,73]. If patients treated with ABMT I & II start to relapse, then patients would need to be randomised to either the double protocol as at present or to a protocol in which the pre ABMT conditioning was changed for ABMT II. I would suggest that the second autograft was then conditioned with either cyclophosphamide and TBI (Thomas et al, 1975)[171] or with cyclophosphamide and busulphan (Yaeger et al, 1986)[189].

Maintenance therapy is probably of no benefit following such intensive regimens and should not be given, particularly as it appears to have increased morbidity as demonstrated in ALL patients in this study (Chapter 8: Morbidity).

RELAPSED PATIENTS

Patients with relapsed AML may be successfully reinduced or consolidated with our current regime without undue morbidity, but there have been no long-term survivors. 4/8 of our patients were harvested in CR1 with no obvious difference in relapse free survival.

Yeager et al, 1986[189], report a 40% long-term survival post ABMT in patients treated with high dose busulphan and cylophosphamide (Bu/Cy) conditioning in a second or

later remission. The autologous marrow was harvested during remission, incubated with 4 hydroperoxycylophosphamide (4HC) and then cryopreserved until the time of reinfusion (Table 33).

TABLE 33. Busulphan and cyclophosphamide regimen as used by Yeager et al, 1986[189].

| DAY | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE 50 MG /KG | * | * | * | * | | |
| BUSULPHAN 1 MG / KG | **** | **** | **** | **** | | |
| ABMT | | | | | | * |

There has been no controlled study to ascertain whether the incubation of the marrow with 4HC is necessary. I would therefore propose a pilot study, whereby the first 10 patients with relapsed AML, who achieve a further CR should be treated with the Bu/Cy regimen but with marrow which has not been incubated with 4HC. The next 10 patients should be treated the same but assuming an adequate harvest, their marrow should be halved and they should go on to a double ABMT. The second ABMT being with our regimen, which uses different drugs and should therefore reduce the risk of drug resistance

developing. It also appears to be less toxic and is therefore likely to be better tolerated as a second procedure (Figure 19).

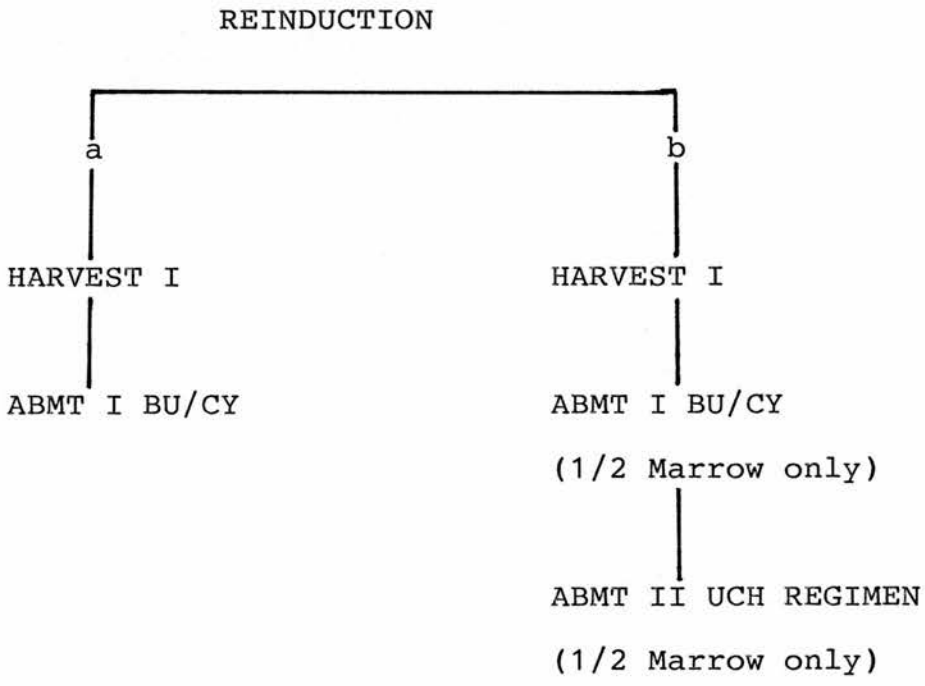



Figure 19. Treatment plan for patients with relapsed AML a) first 10 patients b) next 10 patients.

This should be useful in determining:

(1) Whether it is the conditioning regimen which has resulted in the better DFS post ABMT with Bu/Cy or whether it is the incubation with 4HC of the harvested marrow.

(2) Whether a double ABMT is likely to result in better DFS than a single one.

This pilot study should further indicate whether incubation with 4HC is significantly prolonging haematological recovery. If the median time to recovery of neutrophils $>0.5x10^9/L$ and platelets to $>50x10^9/L$ reported by Yeager et al, is compared with our own results, being 29 and 57 days and 22 and 33 days respectively, then it would seem likely this is the case. (Chapter 7: Haematological recovery). This prolongation in recovery may be responsible for the increase in mortality in the purged group.

It would be interesting to compare the results of ABMT in CR2 with marrow which had been collected either in CR1 or CR2. This would give some idea as to the relative efficacy of the conditioning regimen to eradicate host disease.

This sort of study would only be of value to assess this problem because it would not be possible to store large numbers of patients CR1 marrow, and current results would suggest it is in the patients interest to proceed to ABMT during CR1.

The median time to relapse in all our patients treated after 1st CR and of the 6 patients who relapsed after

Bu/Cy reported by Yaeger et al, 1986[189], was 165 days in both groups. It would therefore, become rapidly evident whether this regimen was proving better than our present protocol or at least as good as the results of Yeager et al. If Bu/Cy was demonstrated to produce improved results in relapsed patients compared to our current double ABMT regimen then it would merit evaluation in first remission patients, as a single ABMT regimen, with or without purging.

As in CR1 patients it may be useful to consider 2 harvests pre ABMT I, or even halving the first harvest, although the same objections as discussed before would arise. In relapsed patients either of these two manouvres would result in the loss of any possible 'in vivo' purging effect of the double autograft. Theoretically, this is the very situation such an effect would be of most value.

## FIRST REMISSION PATIENTS

Our results in 1st CR are very disappointing with 7 of 8 patients dead or relapsed, suggesting our current approach is not useful. We have used the same regimen in ALL as in AML but have encountered a marked increase in morbidity. It is possible that the difference in morbidity between patients with AML and ALL treated on our regimen may be due to either the steroids employed during induction therapy or else the CNS irradiation.

I would like to test this theory by treating a small pilot group of patients with our current ABMT protocol after induction therapy which had no steroids in it and who had only intrathecal treatment for CNS prophylaxis (Figure 20).

If the morbidity was reduced after not using steroids and cranial irradiation, I would then wish to investigate escalation of the drugs used in an effort to reduce the relapse rate. BCNU has produced little non-haematological toxicity as a single agent until doses in excess of 1200 $mg/m^2$ (Herzig et al, 1981)[88] were used and no relevant non-haematological toxicity was reported in adults given $1000mg/m^2$ followed by ABMT (Brun del Re, 1986)[27] or when

used in combination regimens at 800mg/$m^2$ (Meloni et al, 1986)[121]. The cyclophosphamide could probably also be increased without undue toxicity (Table 34).

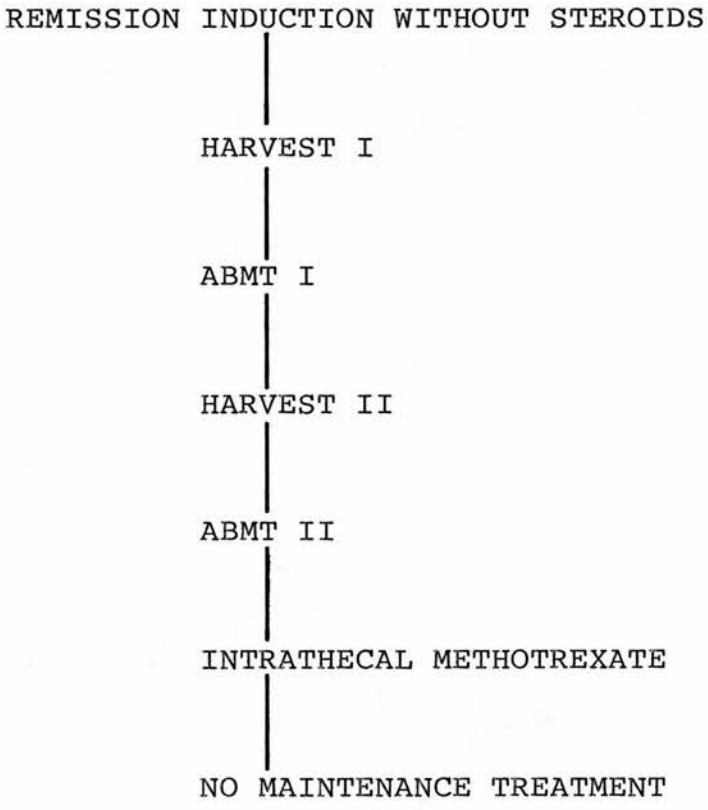



Figure 20. Treatment plan for ALL in CR1 if using the current pre ABMT conditioning regimen.

However, better relapse free survival in patients with ALL has been reported after TBI regimens, than after our protocol (Gorin & Aegerter, 1986)[80]. It would therefore seem inappropriate to initiate any further studies on our current ABMT protocol in ALL patients.

Table 34. Proposed changes ( ) in the UCH chemotherapy regimen (ABMT I & II) for patients with ALL.

| DAY | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE | * | * | * | (*) | | |
| 1.5 G / $M^2$ | | | | | | |
| BCNU | * | (*) | | | | |
| 300 MG / $M^2$ | | | | | | |
| CYTOSINE ARABINOSIDE | ** | ** | ** | ** | | |
| 100 MG / $M^2$ | | | | | | |
| THIOGUANINE | ** | ** | ** | ** | | |
| 100 MG / $M^2$ | | | | | | |
| ADRIAMYCIN | * | | | | | |
| 50 MG / $M^2$ | | | | | | |
| ABMT | | | | | | * |

Most patients will be referred for treatment after they have already been induced. These patients should not be treated with our current regimen. Santos et al, 1986 [126], gave high dose cyclophosphamide (50mg/$m^2$ x 4) followed by TBI (3 gray x 4) to condition patients with ALL in first or second CR pre-allograft, this regimen appears to have a very low relapse rate (1/39). I would propose that this is used as a single ABMT regimen in patients in CR1, until it is seen whether or not it is associated with as high a morbidity as our double

protocol. A further group should be treated with the Bu/Cy regimen (Figure 21).

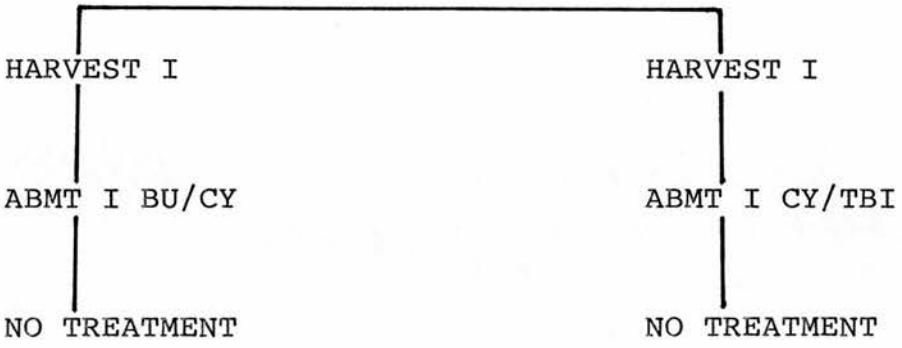



Figure 21. Proposed treatment plan for patients with ALL in CR1 - Single ABMT.

There should be no maintenance therapy post ABMT for ALL as there is no clear benefit, but there is an apparent increase in infective morbidity (Chapter 8: Morbidity).

RELAPSED PATIENTS

Although allogeneic BMT may offer the best currently available hope of long-term survival after relapse only about 30% of patients will have a suitable sibling donor. Autologous transplantation may offer an alternative. Relapse rates are high following allogeneic transplantation, it might therefore be anticipated that the

relapse rate will be even higher if the same preparative regimen is used with the return of autologous marrow, as a proportion of leukaemic cells may be reinfused with the marrow innoculum, and there will be no graft-versus-leukaemia effect (Weiden et al, 1979 & 1981)[181,182,183].

In relapsed patients with ALL our ABMT regimen was successful in achieving a CR but although 6 had both ABMT I and II only 2 patients remain in CR, one of whom has now been in 2nd CR for longer than her original marrow was stored and the 2nd is a girl who had already had 2 CNS relapses as well as a marrow relapse, all the remaining patients relapsed again within 12 months.

Numbers in ABMT studies are generally small and follow up relatively short. The latest EBMTG report (Gorin & Aegerter, 1986)[80] demonstrates no difference in survival for patients with ALL whether treated in CR1 or CR2 and no significant benefit has yet been demonstrated for purging. 2 year survival is 48%. Most of these patients (79%) were treated with a TBI regimen.

I would recommend that ABMT regimens for relapsed patients with ALL, should be the same in CR2 as proposed for use in CR1 (Figure 21).

If both the high dose cyclophosphamide with TBI and the BU/Cy protocols are well tolerated by patients

treated in CR1 and CR2, then a second autograft should be considered, crossing over the two conditioning regimens (Figure 22).

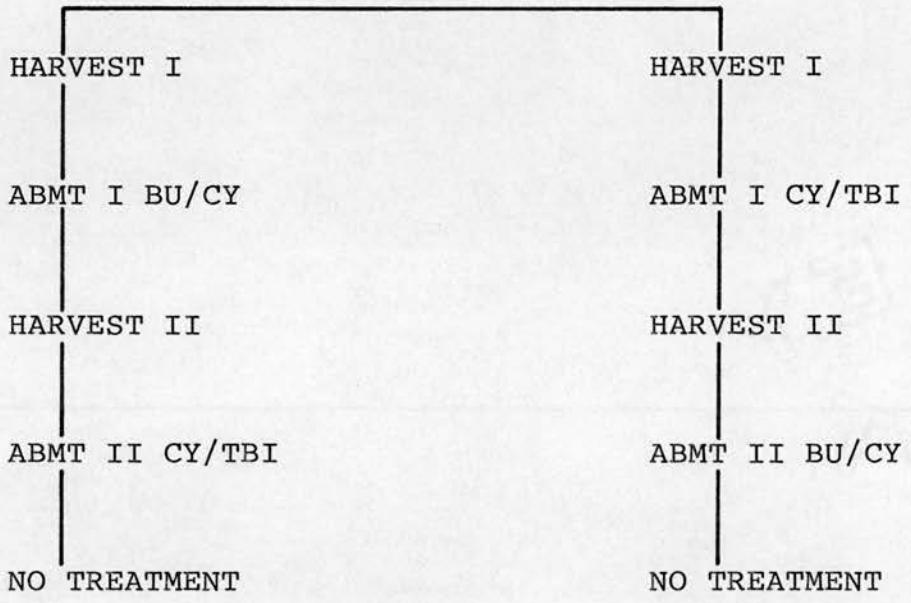



Figure 22. Proposed plan of treatment for patients with ALL in CR1 and CR2 - Double ABMT.

Purging autologous marrow in ALL patients is undergoing extensive investigation. One such recent study (Ramsay et al, 1985)[136] in which the bone marrow of 23 patients in a 2nd or subsequent remission for ALL was harvested and purged 'in vitro' with monoclonal antibodies plus complement reports that 7 remain disease free with a median follow-up of 21.4 months. Purging may need to be considered if benefit is demonstrated in the future.

To assess the place of intensive chemoradiotherapy regimens with ABMT in the treatment of NHL is difficult. The use of regimens to intensify treatment has proved of only limited success where the patient was already deemed resistant to conventional combination chemotherapy (Philip et al, 1985)[129]. In our series 10 patients with resistant relapse were treated, 6 had no response, 1 a PR, 1 a CR and two were non-evaluable because of early death. It may be that after the use of more intensive induction regimens as being currently evaluated, further escalation of therapy with or without marrow rescue may not prove beneficial where the patients have primary resistant disease or relapse has occurred.

The situation is further complicated by having no international agreement on the histological classification of this very heterogeneous group of non-Hodgkin's lymphomas, so results are difficult to compare. The most recent attempt to arrive at an internationally agreed classification is the NCI working formulation (Rosenberg et al, 1982)[146].

A further difficulty in assessing the results of current regimens is that patients with different stages of disease, including stages IB and IIB, have been included in some of the recent trials.

It can be seen from Table 35, that different stages of disease in the BNLI patients are associated with a very different prognosis. (G. Vaughan Hudson, 1986, personal communication)

Table 35. Response to CHOP in 428 patients

BNLI April 1986 (unpublished data)

| STAGE | CR | 5 YEAR RELAPSE FREE SURVIVAL |
|---|---|---|
| II (Nodal) | 67% | 55% |
| IIIA | 72% | 49% |
| IVA | 50% | 32% |
| IIIB | 45% | 23% |
| IVB | 30% | 16% |

It has been suggested that high grade NHL's with poor prognosis should be consolidated with ABMT during CR1. The difficulty has always been to define these poor prognosis categories.

The BNLI have identified various factors in their CHOP study, that have predictive value as to whether CR will be obtained. Once a CR has been obtained however, these factors are of less significance, and patients achieving a CR on CHOP have a 5 year survival of 68% (DC Linch et

al, 1986)[109]. If this is true of other therapeutic regimens, ABMT is not appropriate to consolidate these patients.

Patients with NHL who fail to achieve a CR on first line treatment (primary treatment failures) have a particularly bad prognosis. Many of these patients are in poor clinical condition at the end of attempted remission induction. The BNLI have identified that patients not in CR after 3/12 of treatment have only a 25% 5 year survival. This group of patients would therefore be suitable for alternative treatment at this stage, high dose chemoradiotherapy with ABMT being one of the possibilities.

Relapse occurring either on primary treatment or after its cessation is also a group with poor long-term survival. ABMT may be preferable to conventional second line treatment in this situation.

The BNLI is at present investigating the use of ABMT in both the above situations.

The appropriate regimen to achieve eradication of relapsed disease has not yet been found. The early incidence of relapse in previously involved sites suggests failure to eradicate host disease is the primary cause of relapse and not occult disease reinfused with

the marrow innoculum. In an effort to increase tumour kill, it would seem appropriate to recommend a second cycle of intensive chemoradiotherapy with ABMT rescue as soon as possible on recovery from the first cycle (Figure 23). The second treatment regimen should be composed of different cytotoxic agents to prevent the selection of resistant cells. The marrow collected before the first cycle of cytotoxic agents could be divided if there was an initial cell count of $>2.0x10^8$ cells/kg body weight, but should be repeated if the cell count is less.

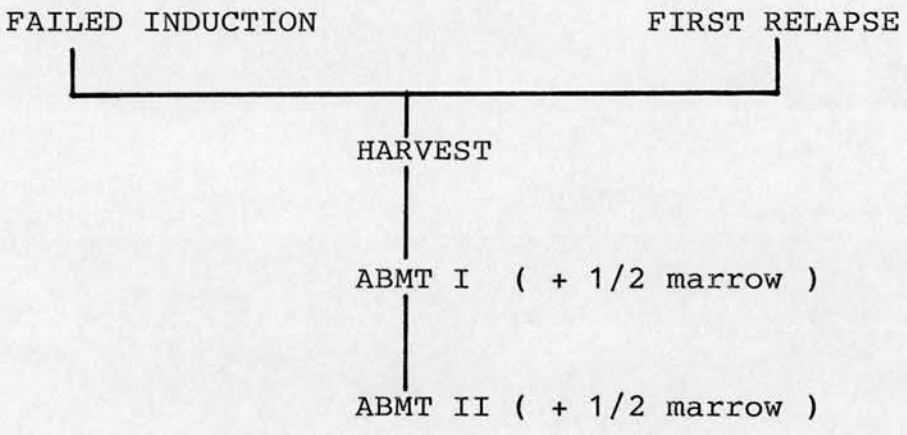



Figure 23. Treatment plan for patients with NHL.

The numbers treated with a double ABMT protocol in our study are too small to draw any conclusions and there are no other reports of the use of a double ABMT protocol in the treatment of lymphoma. However, our own data on the use of a double protocol in patients with AML in CR1 is

encouraging.

I would propose that the conditioning regimen for ABMT I should be the present BNLI protocol but with adriamycin included as in our protocol for patients with acute leukaemia. Adriamycin has been shown in animal studies to be synergistic with cyclophosphamide (Tobias et al, 1975)[177]. The BEAM protocol with adriamycin added could be used as the conditioning regimen for ABMT II (Table 36).

I suspect that even such a double regimen as proposed will not be adequate in patients with advanced relapsed disease and these patients should not be autografted. If the toxicity of the above regimen is no higher than our present protocol I would investigate increasing the dose of the individual drugs employed in the regimen.

Table 36. BNLI & BEAM protocols with added adriamycin.

| ABMT I | DAY | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| CYCLOPHOSPHAMIDE | | * | * | * | * | | |
| 1.5 G / $M^2$ | | | | | | | |
| BCNU | | * | (*) | | | | |
| 300 MG / $M^2$ | | | | | | | |
| CYTOSINE ARABINOSIDE | | ** | ** | ** | ** | | |
| 100 MG / $M^2$ | | | | | | | |
| VP16 | | * | * | * | * | | |
| 75 MG / $M^2$ ( 100 MG / $M^2$ ) | | | | | | | |
| ADRIAMYCIN | | * | | | | | |
| 50 MG / $M^2$ | | | | | | | |
| ABMT | | | | | | | * |

| ABMT II | DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|---|
| BCNU | | * | (*) | | | | | |
| 300 MG / $M^2$ | | | | | | | | |
| CYTOSINE ARABINOSIDE | | ** | ** | ** | ** | | | |
| 100 MG / $M^2$ | | | | | | | | |
| VP16 | | ** | ** | ** | ** | | | |
| 50 MG / $M^2$ | | | | | | | | |
| MELPHALAN | | | | | | | * | |
| 140 MG / $M^2$ | | | | | | | | |
| ADRIAMYCIN | | * | | | | | | |
| 50 MG / $M^2$ | | | | | | | | |
| ABMT | | | | | | | | * |

( ) represent the proposed change in drug dosage.

In the BNLI protocol it is likely that both the BCNU and VP16 doses could be increased to a total dose of 600 $mg/m^2$ and 400 $mg/m^2$ respectively without an undue increase in the non-marrow toxicity. Meloni et al, 1986[121], have used a high dose chemotherapy regimen consisting of 800 $mg/m^2$ BCNU, 450 $mg/m^2$ AMSA, 450 $mg/m^2$ VP16 and cytosine arabinoside 900 $mg/m^2$ as the conditioning regimen for ABMT I in a double protocol to treat 3 patients with AML in relapse. They report no relevant non-haematological complications. The BCNU in the BEAM regimen could be increased to the same extent.

If the conditioning regimen can be altered to achieve eradication of host disease without an unacceptable increase in non-marrow toxicity then bone marrow transplantation particularly ABMT may have a place in the future treatment of patients with advanced diffuse NHL.

In our own series of 15 heavily pre-treated patients with relapsed HD who were treated with intensive chemo-radiotherapy regimens there was a 100% response rate in evaluable patients. One patient was not evaluable owing to an early septicaemic death. There were 11 CRs and 3 PRs. 3 patients have died whilst apparently in CR. Only four patients remain alive in unmaintained CR 7, 7, 17 and 29 months post ABMT. The EBMTG report a similar response rate of 92% for patients with HD treated with various high dose chemoradiotherapy regimens followed by ABMT (63% CR; 29% PR). Overall survival is however, only about 40% (AH Goldstone, 1986)[74].

It is clear that even heavily pre-treated patients with HD remain sensitive to this form of dose escalation. All studies at present employing intensive regimens with bone marrow rescue would tend to suggest that in the relapsed, heavily pre-treated patients the chemoradio-therapy regimens employed although valuable are failing to eradicate host disease in most patients. There is considerable toxicity of this form of treatment. This might be reduced and greater success at eradicating the disease might be obtained by using intensive chemo-radiotherapy earlier in the course of the disease when patients would be better able to physically tolerate the

therapy and the disease would be less resistant to the cytotoxic regimen employed, as has already been demonstrated to be beneficial in patients treated by allografting for acute myeloid leukaemia (Thomas ED, 1983)[169].

There is as yet no obvious stage at which patients with HD should be autografted. This is because survival in patients with HD, even those who are destined to ultimately die of their disease, is generally longer than in patients with acute leukaemia or NHL.

Poor prognostic groups can be identified, such as patients failing after 2 courses of treatment. These patients have a 5 year survival of only 34%, nonetheless they have a median survival which is more than 2 years (Linch et al, 1986)[109]. It would therefore seem appropriate to initiate randomised studies to compare the use of ABMT in the following situation: Failure of 2 treatment regimens ie either primary failure or at second relapse (Figure 24).

The only absolute contraindication to ABMT is marrow involvement, as no suitable method of purging the autologous marrow is yet available in HD, but if a further CR can be induced then ABMT may be considered for consolidation.

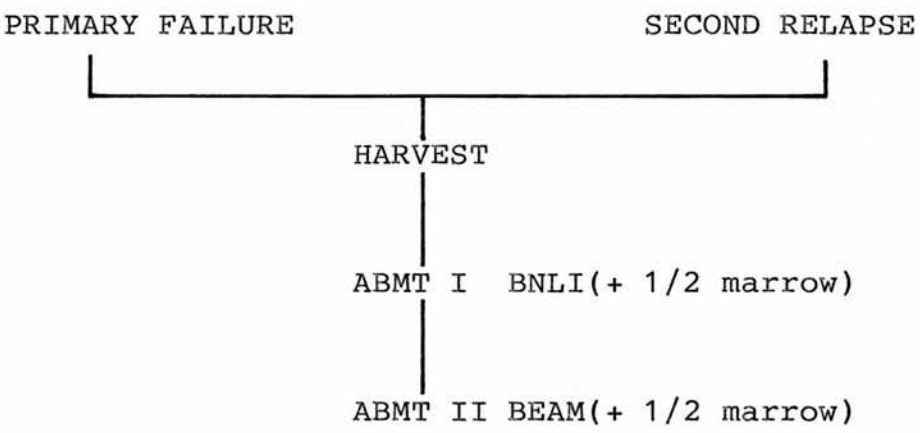



Figure 24. Treatment plan for patients with HD.

Because of the high number of patients who will have had prior DXT, particularly mantle DXT and the high complication rate reported in series utilising TBI (Buckner et al, 1982; Appelbaum et al, 1985)[28,10], TBI is probably best avoided in both the regimens for allografting and autografting.

The relapse rate following intensive chemoradiotherapy and ABMT in patients with advanced disease, is still high, therefore in patients undergoing treatment following 2 or more non-cross-resistant regimens, the intention should be to use a double cycle of high dose chemotherapy with ABMT rescue. I would suggest using the BNLI protocol followed by the BEAM protocol both with additional adriamycin as proposed for use in patients with NHL (Figure 24). The two protocols being used for either ABMT I or II, with patients being randomised to

which they receive first. The inclusion of adriamycin (Table 36) in the regimen for treating patients with HD is likely to be beneficial although many patients with HD will now have received this drug as part of their first line therapy.

The high success rate of conventional regimens in inducing a CR in the majority of patients, and their relatively low toxicity, suggests that there is no place for this intensive form of therapy as primary treatment of HD at the present time. Intensive chemoradiotherapy has a small but significant mortality. If the morbidity/mortality is reduced by its use earlier in the course of the disease and its use is demonstrated to improve survival in the two situations already suggested then the next step might be to randomise patients at first relapse to either ABMT or other second line treatment.

## CONCLUSION

ABMT allows escalation of the dose of cytotoxic agents which can successfully be administered at a single time, with a substantial improvement in the immediate response rate. This form of treatment is complete in a relatively short period of time which is an advantage when compared to the extended treatment period of most current intensive chemotherapy regimes not employing ABMT. ABMT

regimens currently employed cause much less morbidity than allograft regimes, particularly in relation to the absence of GVHD and they are therefore applicable to a much wider patient population. Unless current research leads to the successful elimination of GVHD, I would envisage the use of ABMT to extend the treatment of haematological malignancies will expand rapidly in the future and displace allografting for most of these diseases.

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# APPENDIX I

## PATIENT DATA - ACUTE LEUKAEMIA

ABBREVIATIONS

NA, Data not available.

PP, Private patient.

QE Hospital, Queen Elizabeth Hospital.

SEX:

M, male; F, female.

DIAGNOSIS:

AML, Acute Myeloid Leukaemia; ALL, Acute Lymphoblastic Leukaemia.

CLASSIFICATION:

This is by the French, American, British Classification (Bennett et al, 1976)[15] together with the immunological markers where available.

DXT; Radiotherapy.

IT MTX; Intrathecal methotrexate.

STATUS AT TIME OF ABMT:

1st CR, first complete remission; 2nd CR, second complete remission; 3rd CR, third complete remission.

STATUS POST ABMT:

CR, Complete Remission; NE, Not Evaluable.

OTHER BLOOD PRODUCTS USED:

PPF, Purified Protein Fraction.

FFP, Fresh Frozen Plasma.

Cryo, Cryoprecipitate.

MICROBIOLOGY:

Coag -ve staph, Coagulase negative staphylococci

H.S., Hickman entry site.

Pseud, Pseudomonas

E coli, Escherichia coli

H tip, Hickman tip

a haem strep, a haemolytic streptococcus

B haem strep, B haemolytic streptococcus

Cl, Clostridium

Staph, staphylococcus

sp., species.

Strep, streptococcus

Kleb, klebsiella

Haem, haemophilus

Gp B, Group B

PV, per vaginum.

CNS, central nervous system.

LVF, left ventricular failure.

| | |
|---|---|
| UNIQUE PATIENT NUMBER | : 19 |
| PATIENT NAME | : G TANNER |
| HOSPITAL NUMBER | : AX5090 |
| DATE OF BIRTH | : 12.2.56 |
| AGE IN YEARS | : 25 |
| SEX | : MALE |
| DIAGNOSIS | : AML |
| CLASSIFICATION | : M1 |
| DATE OF DIAGNOSIS | : 15.9.80 |
| DATE OF 1ST CR | : 10.11.80 |
| DATE OF CR PRE-ABMT | : 10.11.80 |
| STATUS AT TIME OF 1ST HARVEST | : 1ST CR |
| DATE OF HARVEST | I : 30.12.80 |
| DATE OF HARVEST | II: 25.2.81 |
| STATUS AT TIME OF ABMT | I : 1ST CR |
| DATE OF ABMT | I : 6.1.81 |
| DATE OF ABMT | II: 6.3.81 |
| NUCLEATED CELL COUNT X $10^8$/KG | I : 3.1 |
| NUCLEATED CELL COUNT X $10^8$/KG | II: 1.7 |
| GM CFC X $10^4$/KG | I : 1.66 |
| GM CFC X $10^4$/KG | II: 1.28 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : 12 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: 13 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : 20 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: 17 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : 17 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: 26 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 18 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: (26-47) |
| LENGTH OF ADMISSION IN DAYS | I : 29 |
| LENGTH OF ADMISSION IN DAYS | II: 33 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 6 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 9 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 5 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 0 |
| NO. OF ANTIBIOTICS USED | I : 3 |
| NO. OF ANTIBIOTICS USED | II: 1 |
| NO. OF UNITS OF BLOOD | I : 8 |
| NO. OF UNITS OF BLOOD | II: 15 |
| NO. OF UNITS OF PLATELETS USED | I : 84 |
| NO. OF UNITS OF PLATELETS USED | II: 38 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : 5 |
| WEIGHT LOSS IN KG | II: NA |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | SALMONELLA INFECTION |
| COMPLICATIONS DURING ABMT | II: | NIL OF NOTE |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Salmonella sp; Faeces/Staph albus; Blood/Candida; Throat |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Salmonella sp; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | IT MTX |
| COMPLICATIONS POST ABMT | : | NIL OF NOTE |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | |
|---|---|
| UNIQUE PATIENT NUMBER | : 30 |
| PATIENT NAME | : O SAID |
| HOSPITAL NUMBER | : PP |
| DATE OF BIRTH | : 11.6.43 |
| AGE IN YEARS | : 38 |
| SEX | : MALE |
| DIAGNOSIS | : AML |
| CLASSIFICATION | : M3 |
| DATE OF DIAGNOSIS | : 12.11.80 |
| DATE OF 1ST CR | : 15.12.80 |
| DATE OF CR PRE-ABMT | : 15.12.80 |
| STATUS AT TIME OF 1ST HARVEST | : 1ST CR |
| DATE OF HARVEST | I : 12.7.81 |
| DATE OF HARVEST | II: NOT DONE |
| STATUS AT TIME OF ABMT | I : 1ST CR |
| DATE OF ABMT | I : 21.7.81 |
| DATE OF ABMT | II: NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I : 1.9 |
| NUCLEATED CELL COUNT X $10^8$/KG | II: |
| GM CFC X $10^4$/KG | I : NA |
| GM CFC X $10^4$/KG | II: |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : 14 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : 22 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/ L | II: |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : 26 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : (27-70) |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 37 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : NA |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : NA |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 5 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : NA |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : NA |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : GRANULOCYTES 7 DAYS |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : NA |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NA |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | ECTHYMA GANGRENOSUM CHEST WALL |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Strep faecalis; Faeces/Strep mitis; Blood/E coli, Strep viridans; Throat/ Pseud aerogenes; H.S., H. tip |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NONE |
| COMPLICATIONS POST ABMT | : | NIL OF NOTE |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 39 |
| PATIENT NAME | | : M INSTRALL |
| HOSPITAL NUMBER | | : BZ0417 |
| DATE OF BIRTH | | : 6.2.62 |
| AGE IN YEARS | | : 19 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : NOT KNOWN |
| DATE OF DIAGNOSIS | | : 27.2.79 |
| DATE OF 1ST CR | | : 26.3.79 |
| DATE OF CR PRE-ABMT | | : 26.3.79 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 28.2.80 |
| DATE OF HARVEST | II | : 21.1.82 |
| STATUS AT TIME OF ABMT | I | : 1ST RELAPSE |
| DATE OF ABMT | I | : 17.11.81 |
| DATE OF ABMT | II | : 27.1.82 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.4 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : NA |
| GM CFC X $10^4$/KG | I | : 4.49 |
| GM CFC X $10^4$/KG | II | : 6.44 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 14 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 17 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 20 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 28 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 20 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 35 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 24 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 61 |
| LENGTH OF ADMISSION IN DAYS | I : 25 |
| LENGTH OF ADMISSION IN DAYS | II: 32 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 10 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 5 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 5 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 2 |
| NO. OF ANTIBIOTICS USED | I : 2 |
| NO. OF ANTIBIOTICS USED | II: 3 |
| NO. OF UNITS OF BLOOD | I : 4 |
| NO. OF UNITS OF BLOOD | II: 8 |
| NO. OF UNITS OF PLATELETS USED | I : 42 |
| NO. OF UNITS OF PLATELETS USED | II: 54 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : 5.3 |
| WEIGHT LOSS IN KG | II: 4 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I | : NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II | : NIL OF NOTE |
| POSITIVE MICROBIOLOGY ISOLATES | I | : Coag -ve staph, Bacteroides fragilis, Cl welchii & butyricum; Faeces/ Staph aureus; Nose |
| POSITIVE MICROBIOLOGY ISOLATES | II | : Cl difficile; Faeces |

| | |
|---|---|
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : MAINTENANCE TREATMENT |
| COMPLICATIONS POST ABMT | : NIL |
| DATE OF RELAPSE | : 12.5.82 |
| SITE OF RELAPSE | : MEDULLARY |
| DATE OF DEATH | : 5.8.82 |
| CAUSE OF DEATH | : ALL |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 41 |
| PATIENT NAME | | : E BROOKES |
| HOSPITAL NUMBER | | : EX0574 |
| DATE OF BIRTH | | : 27.6.24 |
| AGE IN YEARS | | : 57 |
| SEX | | : F |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M2 |
| DATE OF DIAGNOSIS | | : 25.2.80 |
| DATE OF 1ST CR | | : 9.4.80 |
| DATE OF CR PRE-ABMT | | : 9.4.80 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 18.5.81 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST RELAPSE |
| DATE OF ABMT | I | : 5.12.81 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 0.6 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 23 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 25 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 99 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 141 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 43 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 12 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 9 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 3 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 12 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 177 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 10 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | DIARRHOEA & VOMITING, HYPONATREMIA, HYPOKALAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat Serratia marascens; Urine |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | |
|---|---|
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : SYMPTOMATIC ONLY |
| COMPLICATIONS POST ABMT | : PROLONGED VOMITING |
| DATE OF RELAPSE | : 18.7.82 |
| SITE OF RELAPSE | : MEDULLARY |
| DATE OF DEATH | : 13.10.82 |
| CAUSE OF DEATH | : AML |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 51 |
| PATIENT NAME | | : G SINCLAIR |
| HOSPITAL NUMBER | | : ES6623 |
| DATE OF BIRTH | | : 7.2.47 |
| AGE IN YEARS | | : 35 |
| SEX | | : F |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL |
| DATE OF DIAGNOSIS | | : APRIL 77 |
| DATE OF 1ST CR | | : 30.5.77 |
| DATE OF CR PRE-ABMT | | : 30.5.77 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 6.3.80 |
| DATE OF HARVEST | II | : 14.6.82 |
| STATUS AT TIME OF ABMT | I | : 1ST RELAPSE |
| DATE OF ABMT | I | : 8.3.82 |
| DATE OF ABMT | II | : 23.6.82 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.9 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : NA |
| GM CFC X $10^4$/KG | I | : 6.9 |
| GM CFC X $10^4$/KG | II | : 3.09 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 20 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 26 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 31 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 28 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 33 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 45 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 45 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 54 |
| LENGTH OF ADMISSION IN DAYS | I : 46 |
| LENGTH OF ADMISSION IN DAYS | II: 46 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 33 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 34 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 28 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 27 |
| NO. OF ANTIBIOTICS USED | I : 10 |
| NO. OF ANTIBIOTICS USED | II: 9 |
| NO. OF UNITS OF BLOOD | I : 18 |
| NO. OF UNITS OF BLOOD | II: 11 |
| NO. OF UNITS OF PLATELETS USED | I : 220 |
| NO. OF UNITS OF PLATELETS USED | II: 100 |
| OTHER BLOOD PRODUCTS USED | I : FFP |
| OTHER BLOOD PRODUCTS USED | II: GRANULOCYTES 5 DAYS |
| WEIGHT LOSS IN KG | I : 9.7 |
| WEIGHT LOSS IN KG | II: 5.5 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: YES |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | CANDIDA SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida torulopsis & tropicalis; Blood/ Candida; Urine, Throat, Faeces/ Bacillus brevis; Blood, H.S., Ulcer/ Gm -ve organism; Blood/Herpes simplex; Mouth |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Coag -ve staph; Blood, H.S./ Strep viridans; Blood /Pseud aerogenes, diphtheroids; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | MAINTENANCE TREATMENT UNTIL JANUARY 1985 |
| COMPLICATIONS POST ABMT | : | CATARACT / LISTERIA SEPTICAEMIA |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 55 |
| PATIENT NAME | | : D SOWDEN |
| HOSPITAL NUMBER | | : EX8523 |
| DATE OF BIRTH | | : 4.12.50 |
| AGE IN YEARS | | : 31 |
| SEX | | : F |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 16.10.81 |
| DATE OF 1ST CR | | : 23.12.81 |
| DATE OF CR PRE-ABMT | | : 4.5.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 2ND CR |
| DATE OF HARVEST | I | : 17.5.82 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 24.5.82 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 29 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 34 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 34 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 38 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 11 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 4 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 3 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 16 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 233 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 4 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | HICKMAN INFECTION / BLEEDING |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Staph aureus; Nose/ /E. coli, Cl difficile; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | |
|---|---|
| STATUS POST ABMT | : RELAPSE |
| TREATMENT POST ABMT | : FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : |
| DATE OF RELAPSE | : 3.7.82 |
| SITE OF RELAPSE | : MEDULLARY |
| DATE OF DEATH | : 19.1.83 |
| CAUSE OF DEATH | : AML |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 57 |
| PATIENT NAME | | : R THANWANI |
| HOSPITAL NUMBER | | : PP |
| DATE OF BIRTH | | : 16.6.59 |
| AGE IN YEARS | | : 23 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : T CELL |
| DATE OF DIAGNOSIS | | : 3.3.82 |
| DATE OF 1ST CR | | : 19.3.82 |
| DATE OF CR PRE-ABMT | | : 19.3.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 18.6.82 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 26.6.82 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 16 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 23 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 25 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |
| LENGTH OF ADMISSION IN DAYS | I : | 35 |
| LENGTH OF ADMISSION IN DAYS | II: | |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : | 22 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: | |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : | 16 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: | |
| NO. OF ANTIBIOTICS USED | I : | 5 |
| NO. OF ANTIBIOTICS USED | II: | |
| NO. OF UNITS OF BLOOD | I : | 4 |
| NO. OF UNITS OF BLOOD | II: | |
| NO. OF UNITS OF PLATELETS USED | I : | 45 |
| NO. OF UNITS OF PLATELETS USED | II: | |
| OTHER BLOOD PRODUCTS USED | I : | GRANULOCYTES 5 DAYS |
| OTHER BLOOD PRODUCTS USED | II: | |
| WEIGHT LOSS IN KG | I : | 5 |
| WEIGHT LOSS IN KG | II: | |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : | YES |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: | |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | HAEMORRHAGIC CYSTITIS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat/ Candida precipitins Weak +ve/Coag -ve staph; H.S./E. coli Faeces/ Pseud aerogenes; Throat |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | |
|---|---|
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : FURTHER CYTOTOXICS / DXT |
| COMPLICATIONS POST ABMT | : |
| DATE OF RELAPSE | : 3.7.82 |
| SITE OF RELAPSE | : CNS |
| DATE OF DEATH | : 11.11.82 |
| CAUSE OF DEATH | : ALL |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 67 |
| PATIENT NAME | | : L BEEBY |
| HOSPITAL NUMBER | | : EX4761 |
| DATE OF BIRTH | | : 30.7.59 |
| AGE IN YEARS | | : 23 |
| SEX | | : F |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : NOT KNOWN |
| DATE OF DIAGNOSIS | | : 17.2.81 |
| DATE OF 1ST CR | | : 15.4.81 |
| DATE OF CR PRE-ABMT | | : 8.9.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 2.8.81 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 18.9.82 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 16 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 22 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 30 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 30 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 17 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 8 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 5 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 8 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 68 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NO |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 1.5 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : YES |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat, Faeces/Coag -ve staph; Throat, H.S./ Pseud aerogenes; Throat |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | |
|---|---|
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : MAINTENANCE CHEMOTHERAPY |
| COMPLICATIONS POST ABMT | : HERPES ZOSTER (T12-L1) OCTOBER 82 |
| DATE OF RELAPSE | : 26.4.83 |
| SITE OF RELAPSE | : MEDULLARY |
| DATE OF DEATH | : 2.6.83 |
| CAUSE OF DEATH | : ALL |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 69 |
| PATIENT NAME | | : C HEAGUE |
| HOSPITAL NUMBER | | : EZ6660 |
| DATE OF BIRTH | | : 27.12.58 |
| AGE IN YEARS | | : 24 |
| SEX | | : F |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : NOT KNOWN |
| DATE OF DIAGNOSIS | | : 19.4.82 |
| DATE OF 1ST CR | | : 10.5.82 |
| DATE OF CR PRE-ABMT | | : 10.5.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 20.9.82 |
| DATE OF HARVEST | II | : 29.11.82 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 27.9.82 |
| DATE OF ABMT | II | : 21.12.82 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.3 |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 21 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 25 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 21 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 25 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 28 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 45 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 36 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 55 |
| LENGTH OF ADMISSION IN DAYS | I : 34 |
| LENGTH OF ADMISSION IN DAYS | II: 74 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 21 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 31 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 16 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 17 |
| NO. OF ANTIBIOTICS USED | I : 6 |
| NO. OF ANTIBIOTICS USED | II: 10 |
| NO. OF UNITS OF BLOOD | I : 8 |
| NO. OF UNITS OF BLOOD | II: 22 |
| NO. OF UNITS OF PLATELETS USED | I : 59 |
| NO. OF UNITS OF PLATELETS USED | II: 157 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: PPF |
| WEIGHT LOSS IN KG | I : 2.1 |
| WEIGHT LOSS IN KG | II: 0.5 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : YES |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: YES |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | PULMONARY ASPERGILLOMA |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S./ Candida; Throat/Cl. difficile; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Coag -ve staph; Throat, H.S./E coli; Urine,Faeces/Candida; Faeces,Throat,Sputum |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS / DXT |
| COMPLICATIONS POST ABMT | : | FIBROTIC LUNG ? AETIOLOGY |
| DATE OF RELAPSE | : | 10.1.85 |
| SITE OF RELAPSE | : | EXTRAMEDULLARY - BREAST LUMP |
| DATE OF DEATH | : | 25.4.85 |
| CAUSE OF DEATH | : | ALL |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 90 |
| PATIENT NAME | | : S AlROWAITHEY |
| HOSPITAL NUMBER | | : EZ9359 |
| DATE OF BIRTH | | : 17.12.75 |
| AGE IN YEARS | | : 6 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : T CELL |
| DATE OF DIAGNOSIS | | : 18.9.82 |
| DATE OF 1ST CR | | : 11.10.82 |
| DATE OF CR PRE-ABMT | | : NA |
| STATUS AT TIME OF 1ST HARVEST | | : 2ND CR |
| DATE OF HARVEST | I | : 4.2.83 |
| DATE OF HARVEST | II | : 19.4.83 |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 7.3.83 |
| DATE OF ABMT | II | : 26.4.83 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 0.68 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 4.04 |
| GM CFC X $10^4$/KG | I | : 27.5 |
| GM CFC X $10^4$/KG | II | : 15.3 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 14 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 13 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 17 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 27 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 18 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 36 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 21 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 41 |
| LENGTH OF ADMISSION IN DAYS | I : 26 |
| LENGTH OF ADMISSION IN DAYS | II: 34 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 17 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 13 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 6 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 7 |
| NO. OF ANTIBIOTICS USED | I : 4 |
| NO. OF ANTIBIOTICS USED | II: 2 |
| NO. OF UNITS OF BLOOD | I : 3 |
| NO. OF UNITS OF BLOOD | II: 4 |
| NO. OF UNITS OF PLATELETS USED | I : 27 |
| NO. OF UNITS OF PLATELETS USED | II: 45 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : NA |
| WEIGHT LOSS IN KG | II: 4 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NA |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S./ Strep sanguis; Blood/ E coli, Cl difficile + Toxin; Faeces/ Candida; Mouth, Throat, Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Coag -ve staph; Blood /Staph aureus; Nose/ E coli, Cl difficile; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 24.6.83 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 7.11.83 |
| CAUSE OF DEATH | : | ALL |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 92 |
| PATIENT NAME | | : W ACERS |
| HOSPITAL NUMBER | | : EZ4296 |
| DATE OF BIRTH | | : 19.7.33 |
| AGE IN YEARS | | : 49 |
| SEX | | : M |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 16.2.81 |
| DATE OF 1ST CR | | : 28.5.81 |
| DATE OF CR PRE-ABMT | | : 28.5.81 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 12.7.82 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST RELAPSE |
| DATE OF ABMT | I | : 23.3.83 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : NEVER |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 61 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 61 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 39 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 9 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 5 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 48 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : GRANULOCYTES 5 DAYS |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 7.15 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NECK HAEMATOMA / INFECTION |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; Neck, H.S./Candida; Throat, Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | DEAD |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 4.4.83 |
| CAUSE OF DEATH | : | INTRACEREBRAL HAEMORRHAGE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 96 |
| PATIENT NAME | | : K GOVIND |
| HOSPITAL NUMBER | | : EX3885 |
| DATE OF BIRTH | | : 11.6.59 |
| AGE IN YEARS | | : 23 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL |
| DATE OF DIAGNOSIS | | : 17.12.80 |
| DATE OF 1ST CR | | : 8.1.81 |
| DATE OF CR PRE-ABMT | | : 27.3.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 20.7.81 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 21.4.83 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 18 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 18 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 33 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 41 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 35 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 10 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 6 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 6 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 4 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 69 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : PPF / FFP |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 0 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | GRAM -VE SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Kleb aerogenes; Blood, Urine, Faeces/ Strep faecalis; Blood, H.S./Candida; Throat, Faeces/Herpes simplex; mouth/ Coag -ve staph, diphtheroids; H.S./ Cl difficile; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 29.6.83 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 25.8.83 |
| CAUSE OF DEATH | : | ALL |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 98 |
| PATIENT NAME | | : A GALLO |
| HOSPITAL NUMBER | | : EZ5711 |
| DATE OF BIRTH | | : 7.2.39 |
| AGE IN YEARS | | : 44 |
| SEX | | : M |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 7.7.82 |
| DATE OF 1ST CR | | : 4.1.83 |
| DATE OF CR PRE-ABMT | | : 13.4.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 2ND CR |
| DATE OF HARVEST | I | : 15.4.83 |
| DATE OF HARVEST | II | : 15.7.83 |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 9.5.83 |
| DATE OF ABMT | II | : 23.7.83 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.3 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : NA |
| GM CFC X $10^4$/KG | I | : 1.09 |
| GM CFC X $10^4$/KG | II | : 0.87 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 13 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 25 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 17 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 32 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 28 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 51 |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 37

DAYS UNTIL PLATELETS >100 X $10^9$/L II: NEVER

LENGTH OF ADMISSION IN DAYS I : 24

LENGTH OF ADMISSION IN DAYS II: 45

NO. OF DAYS TEMP. > 37.2$^0$C I : 11

NO. OF DAYS TEMP. > 37.2$^0$C II: 20

NO. OF DAYS TEMP. > 38.0$^0$C I : 3

NO. OF DAYS TEMP. > 38.0$^0$C II: 10

NO. OF ANTIBIOTICS USED I : 3

NO. OF ANTIBIOTICS USED II: 4

NO. OF UNITS OF BLOOD I : 4

NO. OF UNITS OF BLOOD II: 7

NO. OF UNITS OF PLATELETS USED I : 41

NO. OF UNITS OF PLATELETS USED II: 127

OTHER BLOOD PRODUCTS USED I : NONE

OTHER BLOOD PRODUCTS USED II: NONE

WEIGHT LOSS IN KG I : 8

WEIGHT LOSS IN KG II: 5

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NO

TOTAL PARENTERAL NUTRITION ADMINISTERED II: NO

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I | : NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II | : NIL OF NOTE |
| POSITIVE MICROBIOLOGY ISOLATES | I | : Herpes simplex; Mouth/Coag -ve staph, diptheroids; H.S./Cl difficile; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II | : Coag -ve staph; H.S./ E coli; Blood, Faeces |
| STATUS POST ABMT | | : CR |
| TREATMENT POST ABMT | | : |
| COMPLICATIONS POST ABMT | | : LUNG INFILTRATES |
| DATE OF RELAPSE | | : 19.1.84 |
| SITE OF RELAPSE | | : MEDULLARY |
| DATE OF DEATH | | : 28.1.84 |
| CAUSE OF DEATH | | : AML |
| CURRENT STATUS | | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 100 |
| PATIENT NAME | | : A ANDREW |
| HOSPITAL NUMBER | | : FB0716 |
| DATE OF BIRTH | | : 8.3.31 |
| AGE IN YEARS | | : 51 |
| SEX | | : M |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M5 |
| DATE OF DIAGNOSIS | | : 30.9.82 |
| DATE OF 1ST CR | | : 23.11.82 |
| DATE OF CR PRE-ABMT | | : 23.11.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 6.5.83 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST RELAPSE |
| DATE OF ABMT | I | : 28.5.83 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.36 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 29 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 33 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 64 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : NEVER

DAYS UNTIL PLATELETS >100 X $10^9$/L II:

LENGTH OF ADMISSION IN DAYS I : 45

LENGTH OF ADMISSION IN DAYS II:

NO. OF DAYS TEMP. > $37.2^0$C I : 13

NO. OF DAYS TEMP. > $37.2^0$C II:

NO. OF DAYS TEMP. > $38.0^0$C I : 6

NO. OF DAYS TEMP. > $38.0^0$C II:

NO. OF ANTIBIOTICS USED I : 4

NO. OF ANTIBIOTICS USED II:

NO. OF UNITS OF BLOOD I : 9

NO. OF UNITS OF BLOOD II:

NO. OF UNITS OF PLATELETS USED I : 125

NO. OF UNITS OF PLATELETS USED II:

OTHER BLOOD PRODUCTS USED I : NONE

OTHER BLOOD PRODUCTS USED II:

WEIGHT LOSS IN KG I : 5

WEIGHT LOSS IN KG II:

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NO

TOTAL PARENTERAL NUTRITION ADMINISTERED II:

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | ABSCESS IN GROIN |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Cl. sporogenes; Blood/Pseud fluorescens; Perineum/Coag -ve staph; H.S./ Serratia marascens; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | |
|---|---|
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : |
| DATE OF RELAPSE | : 18.8.83 |
| SITE OF RELAPSE | : MEDULLARY |
| DATE OF DEATH | : 3.9.83 |
| CAUSE OF DEATH | : AML |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 103 |
| PATIENT NAME | | : R SMITHERS |
| HOSPITAL NUMBER | | : FA0610 |
| DATE OF BIRTH | | : 11.10.67 |
| AGE IN YEARS | | : 16 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL |
| DATE OF DIAGNOSIS | | : OCTOBER 82 |
| DATE OF 1ST CR | | : 2.12.82 |
| DATE OF CR PRE-ABMT | | : 2.12.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 29.4.83 |
| DATE OF HARVEST | II | : 5.8.83 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 12.6.83 |
| DATE OF ABMT | II | : 17.8.83 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.4 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 3.0 |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 13 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 20 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 15 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 21 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 13 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 20 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 15 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 33 |
| LENGTH OF ADMISSION IN DAYS | I : 23 |
| LENGTH OF ADMISSION IN DAYS | II: 27 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 2 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 3 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 0 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 2 |
| NO. OF ANTIBIOTICS USED | I : 0 |
| NO. OF ANTIBIOTICS USED | II: 1 |
| NO. OF UNITS OF BLOOD | I : 2 |
| NO. OF UNITS OF BLOOD | II: 4 |
| NO. OF UNITS OF PLATELETS USED | I : 22 |
| NO. OF UNITS OF PLATELETS USED | II: 26 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : 3 |
| WEIGHT LOSS IN KG | II: 3 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Staph. aureus; Nose |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Coag -ve staph; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | MAINTENANCE TREATMENT |
| COMPLICATIONS POST ABMT | : | NIL |
| DATE OF RELAPSE | : | 20.1.86 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 105 |
| PATIENT NAME | | : D MOSELEY |
| HOSPITAL NUMBER | | : BB6216 |
| DATE OF BIRTH | | : 7.7.39 |
| AGE IN YEARS | | : 43 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M4 |
| DATE OF DIAGNOSIS | | : 27.10.82 |
| DATE OF 1ST CR | | : 10.1.83 |
| DATE OF CR PRE-ABMT | | : 10.1.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 15.4.83 |
| DATE OF HARVEST | II | : 16.9.83 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 27.6.83 |
| DATE OF ABMT | II | : 2.10.83 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.25 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.24 |
| GM CFC X $10^4$/KG | I | : 3.49 |
| GM CFC X $10^4$/KG | II | : 1.69 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 17 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 31 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 18 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 36 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 35 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 36 |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 41

DAYS UNTIL PLATELETS >100 X $10^9$/L II: 74

LENGTH OF ADMISSION IN DAYS I : 25

LENGTH OF ADMISSION IN DAYS II: 36

NO. OF DAYS TEMP. > $37.2^0$C I : 24

NO. OF DAYS TEMP. > $37.2^0$C II: 21

NO. OF DAYS TEMP. > $38.0^0$C I : 0

NO. OF DAYS TEMP. > $38.0^0$C II: 5

NO. OF ANTIBIOTICS USED I : 2

NO. OF ANTIBIOTICS USED II: 5

NO. OF UNITS OF BLOOD I : 6

NO. OF UNITS OF BLOOD II: 6

NO. OF UNITS OF PLATELETS USED I : 23

NO. OF UNITS OF PLATELETS USED II: 56

OTHER BLOOD PRODUCTS USED I : NONE

OTHER BLOOD PRODUCTS USED II: NONE

WEIGHT LOSS IN KG I : 1.6

WEIGHT LOSS IN KG II: 1.9

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NO

TOTAL PARENTERAL NUTRITION ADMINISTERED II: NO

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | PV BLEEDING |
| COMPLICATIONS DURING ABMT | II: | NIL OF NOTE |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Mouth, Throat/Coag -ve staph; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Strep Gp B, diptheroids; H.S. /Candida; Throat, Faeces/Klebsiella oxytocum; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NONE |
| COMPLICATIONS POST ABMT | : | NIL OF NOTE |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 107 |
| PATIENT NAME | | : R CHOUDARI |
| HOSPITAL NUMBER | | : ES5020 |
| DATE OF BIRTH | | : 20.6.36 |
| AGE IN YEARS | | : 47 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL |
| DATE OF DIAGNOSIS | | : 8.2.80 |
| DATE OF 1ST CR | | : 16.4.80 |
| DATE OF CR PRE-ABMT | | : 5.5.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 9.10.80 |
| DATE OF HARVEST | II | : 2.9.83 |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 12.7.83 |
| DATE OF ABMT | II | : 8.9.83 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.6 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : NA |
| GM CFC X $10^4$/KG | I | : 6.32 |
| GM CFC X $10^4$/KG | II | : 3.89 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 13 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 18 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 14 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 18 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 20 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 34 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 20 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: NEVER |
| LENGTH OF ADMISSION IN DAYS | I : 24 |
| LENGTH OF ADMISSION IN DAYS | II: 40 |
| NO. OF DAYS TEMP. > $37.2^0$C | I : 13 |
| NO. OF DAYS TEMP. > $37.2^0$C | II: 23 |
| NO. OF DAYS TEMP. > $38.0^0$C | I : 4 |
| NO. OF DAYS TEMP. > $38.0^0$C | II: 15 |
| NO. OF ANTIBIOTICS USED | I : 4 |
| NO. OF ANTIBIOTICS USED | II: 6 |
| NO. OF UNITS OF BLOOD | I : 5 |
| NO. OF UNITS OF BLOOD | II: 11 |
| NO. OF UNITS OF PLATELETS USED | I : 27 |
| NO. OF UNITS OF PLATELETS USED | II: 110 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : 2 |
| WEIGHT LOSS IN KG | II: 2 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph, Strep milleri; Blood/ Staph aureus; Nose/ E coli; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Coag -ve staph; H.S./ E coli, Cl difficile; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | MAINTENANCE CHEMOTHERAPY |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 15.5.84 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 22.6.84 |
| CAUSE OF DEATH | : | ALL |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 108 |
| PATIENT NAME | | : U PARRY |
| HOSPITAL NUMBER | | : FB3966 |
| DATE OF BIRTH | | : 30.1.44 |
| AGE IN YEARS | | : 39 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 22.10.82 |
| DATE OF 1ST CR | | : 4.12.82 |
| DATE OF CR PRE-ABMT | | : 4.12.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 8.7.83 |
| DATE OF HARVEST | II | : 9.9.83 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 22.7.83 |
| DATE OF ABMT | II | : 17.9.83 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.5 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.9 |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 18 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 41 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 18 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 45 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 20 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 58 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 24 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: (89-144) |
| LENGTH OF ADMISSION IN DAYS | I : 36 |
| LENGTH OF ADMISSION IN DAYS | II: 58 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 20 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 30 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 8 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 11 |
| NO. OF ANTIBIOTICS USED | I : 4 |
| NO. OF ANTIBIOTICS USED | II: 6 |
| NO. OF UNITS OF BLOOD | I : 7 |
| NO. OF UNITS OF BLOOD | II: 19 |
| NO. OF UNITS OF PLATELETS USED | I : 61 |
| NO. OF UNITS OF PLATELETS USED | II: 162 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : 3.4 |
| WEIGHT LOSS IN KG | II: NIL |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II: | NIL OF NOTE |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; Nose, H.S./Herpes simplex; Mouth/ Strep faecalis; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | E coli, Candida, Cl difficile; Faeces/ Acinetobacter sp.; H.S./Candida; Throat |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NONE |
| COMPLICATIONS POST ABMT | : | EARLY MENOPAUSE |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 118 |
| PATIENT NAME | | : S McCARRISON |
| HOSPITAL NUMBER | | : EZ9358 |
| DATE OF BIRTH | | : 23.5.61 |
| AGE IN YEARS | | : 22 |
| SEX | | : F |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : NULL |
| DATE OF DIAGNOSIS | | : 26.3.80 |
| DATE OF 1ST CR | | : 28.5.80 |
| DATE OF CR PRE-ABMT | | : 6.10.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 2ND CR |
| DATE OF HARVEST | I | : 10.6.83 |
| DATE OF HARVEST | II | : 9.12.83 |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 15.10.83 |
| DATE OF ABMT | II | : 26.1.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.35 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.4 |
| GM CFC X $10^4$/KG | I | : 3.06 |
| GM CFC X $10^4$/KG | II | : 3.6 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 20 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 25 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 27 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 25 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 26 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 28 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 28 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 42 |
| LENGTH OF ADMISSION IN DAYS | I : 38 |
| LENGTH OF ADMISSION IN DAYS | II: 33 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 26 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: NA |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 7 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: NA |
| NO. OF ANTIBIOTICS USED | I : 4 |
| NO. OF ANTIBIOTICS USED | II: NA |
| NO. OF UNITS OF BLOOD | I : 8 |
| NO. OF UNITS OF BLOOD | II: NA |
| NO. OF UNITS OF PLATELETS USED | I : 65 |
| NO. OF UNITS OF PLATELETS USED | II: NA |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NA |
| WEIGHT LOSS IN KG | I : NA |
| WEIGHT LOSS IN KG | II: NA |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NA |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S./ E coli; Urine/ Staph aureus; Nose |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Staph aureus; Nose, H.S./Candida; Throat, Faeces/Cl difficile + Toxin; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | MAINTENANCE CHEMOTHERAPY |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 26.7.84 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | MARCH 85 |
| CAUSE OF DEATH | : | ALL |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 121 |
| PATIENT NAME | | : R ROBINSON |
| HOSPITAL NUMBER | | : FB9169 |
| DATE OF BIRTH | | : 3.10.45 |
| AGE IN YEARS | | : 38 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : T CELL |
| DATE OF DIAGNOSIS | | : FEBRUARY 81 |
| DATE OF 1ST CR | | : 16.4.81 |
| DATE OF CR PRE-ABMT | | : 16.4.81 (MEDULLARY) |
| STATUS AT TIME OF 1ST HARVEST | | : 2ND CR (POST TESTICULAR RELAPSE) |
| DATE OF HARVEST | I | : 14.10.83 |
| DATE OF HARVEST | II | : 13.1.84 |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 23.10.83 |
| DATE OF ABMT | II | : 23.1.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.12 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : NA |
| GM CFC X $10^4$/KG | I | : 0.69 |
| GM CFC X $10^4$/KG | II | : 1.42 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 18 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 19 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : NEVER |

| | |
|---|---|
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : 22 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 37 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: NEVER |
| LENGTH OF ADMISSION IN DAYS | I : 33 |
| LENGTH OF ADMISSION IN DAYS | II: 43 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 14 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 25 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 6 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 17 |
| NO. OF ANTIBIOTICS USED | I : 5 |
| NO. OF ANTIBIOTICS USED | II: 11 |
| NO. OF UNITS OF BLOOD | I : 7 |
| NO. OF UNITS OF BLOOD | II: 25 |
| NO. OF UNITS OF PLATELETS USED | I : 37 |
| NO. OF UNITS OF PLATELETS USED | II: 137 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: GRANULOCYTES 5 DAYS/FFP/ CRYO/PPF |
| WEIGHT LOSS IN KG | I : 6 |
| WEIGHT LOSS IN KG | II: 2.8 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : YES |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: YES |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I | : CANDIDA OESOPHAGITIS |
| COMPLICATIONS DURING ABMT | II | : ASPERGILLUS PNEUMONIA |
| POSITIVE MICROBIOLOGY ISOLATES | I | : Pseud aerogenes; Axillary abscess/ Coag -ve staph, diphtheroids; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II | : Strep sanguis & mitis Blood/Coag -ve staph; H.S./Aspergillus fumigatus; Sputum |
| STATUS POST ABMT | | : DEAD |
| TREATMENT POST ABMT | | : |
| COMPLICATIONS POST ABMT | | : |
| DATE OF RELAPSE | | : |
| SITE OF RELAPSE | | : |
| DATE OF DEATH | | : 24.2.84 |
| CAUSE OF DEATH | | : ASPERGILLUS PNEUMONIA |
| CURRENT STATUS | | : DEAD |

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|---|---|
| UNIQUE PATIENT NUMBER | : 122 |
| PATIENT NAME | : Z ALGOHARI |
| HOSPITAL NUMBER | : PP |
| DATE OF BIRTH | : 21.3.49 |
| AGE IN YEARS | : 34 |
| SEX | : F |
| DIAGNOSIS | : AML |
| CLASSIFICATION | : M5 |
| DATE OF DIAGNOSIS | : 7.3.83 |
| DATE OF 1ST CR | : 12.4.83 |
| DATE OF CR PRE-ABMT | : 21.9.83 |
| STATUS AT TIME OF 1ST HARVEST | : 2ND CR |
| DATE OF HARVEST | I : 20.10.83 |
| DATE OF HARVEST | II: NOT DONE |
| STATUS AT TIME OF ABMT | I : 2ND CR |
| DATE OF ABMT | I : 30.10.83 |
| DATE OF ABMT | II: NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II: |
| GM CFC X $10^4$/KG | I : NA |
| GM CFC X $10^4$/KG | II: |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : 18 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : 18 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : 22 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 30 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 26 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 8 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 5 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 7 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 13 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 80 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : NA |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S./Candida, Strep faecalis; Vaginum/ Staph aureus; Vesicle on face |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 12.1.84 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 27.5.84 |
| CAUSE OF DEATH | : | AML |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 125 |
| PATIENT NAME | | : K MARLBOROUGH |
| HOSPITAL NUMBER | | : EV5987 |
| DATE OF BIRTH | | : 8.3.63 |
| AGE IN YEARS | | : 21 |
| SEX | | : M |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 4.8.80 |
| DATE OF 1ST CR | | : 2.10.80 |
| DATE OF CR PRE-ABMT | | : 30.9.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 21.1.81 |
| DATE OF HARVEST | II | : 27.1.84 |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 26.11.83 |
| DATE OF ABMT | II | : 8.2.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.2 |
| GM CFC X $10^4$/KG | I | : 6.23 |
| GM CFC X $10^4$/KG | II | : 0.94 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 21 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 33 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 21 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 33 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 21 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 47 |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 25

DAYS UNTIL PLATELETS >100 X $10^9$/L II: 57

LENGTH OF ADMISSION IN DAYS I : 33

LENGTH OF ADMISSION IN DAYS II: 44

NO. OF DAYS TEMP. > 37.2$^0$C I : NA

NO. OF DAYS TEMP. > 37.2$^0$C II: NA

NO. OF DAYS TEMP. > 38.0$^0$C I : NA

NO. OF DAYS TEMP. > 38.0$^0$C II: NA

NO. OF ANTIBIOTICS USED I : 9

NO. OF ANTIBIOTICS USED II: 5

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II: NA

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II: NA

OTHER BLOOD PRODUCTS USED I : NONE

OTHER BLOOD PRODUCTS USED II: FFP

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II: NA

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II: NA

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | GRAM -VE SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | GRAM -VE SEPTICAEMIA / GASTRO-INTESTINAL BLEEDING |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat, Faeces/Pseud. aerogenes; Blood, Faece/ Coag -ve staph; H.S./Herpes simplex; vesicle |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Candida; Throat, Faeces/Pseud. aerogenes; Blood, Lesion Right elbow/ Coag -ve staph., diphtheroids; H.S |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | SYMPTOMATIC ONLY |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 3.5.84 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 4.6.84 |
| CAUSE OF DEATH | : | AML |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 128 |
| PATIENT NAME | | : G SANKEY |
| HOSPITAL NUMBER | | : FB6334 |
| DATE OF BIRTH | | : 3.4.51 |
| AGE IN YEARS | | : 32 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M2 |
| DATE OF DIAGNOSIS | | : 26.7.83 |
| DATE OF 1ST CR | | : 30.8.83 |
| DATE OF CR PRE-ABMT | | : 30.8.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 2.12.83 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 8.1.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.3 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 40 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 52 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 228 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 494 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 54 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 26 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 17 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 4 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 17 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 177 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 7.4 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Mouth, Throat, Faeces/ Coag -ve staph; H.S./E coli; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NONE |
| COMPLICATIONS POST ABMT | : | ERRATIC MENSTRUATION |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 129 |
| PATIENT NAME | | : J KINGABY |
| HOSPITAL NUMBER | | : FC3996 |
| DATE OF BIRTH | | : 25.6.32 |
| AGE IN YEARS | | : 51 |
| SEX | | : M |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M6 |
| DATE OF DIAGNOSIS | | : 3.1.81 |
| DATE OF 1ST CR | | : 5.2.81 |
| DATE OF CR PRE-ABMT | | : 3.10.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 2ND CR |
| DATE OF HARVEST | I | : 6.1.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 17.1.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.0 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : 5.1 |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 24 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 24 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 37 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 51 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 49 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 20 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 8 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 6 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 8 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 89 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : GRANULOCYTES 6 DAYS |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 9.4 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : YES |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | GM -VE SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Pseud. aerogenes; Blood, mouth, scrotum/Coag -ve staph; H.S. Acinetobacter sp.; Urine |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | REFUSED FURTHER TREATMENT |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 14.2.85 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 1.4.84 |
| CAUSE OF DEATH | : | AML |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 131 |
| PATIENT NAME | | : R HALL |
| HOSPITAL NUMBER | | : FC4539 |
| DATE OF BIRTH | | : 2.6.38 |
| AGE IN YEARS | | : 45 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M4 |
| DATE OF DIAGNOSIS | | : 7.6.83 |
| DATE OF 1ST CR | | : 12.9.83 |
| DATE OF CR PRE-ABMT | | : 12.9.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 27.1.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 6.2.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.6 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 38 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 38 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 64 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 73 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 47 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 21 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 6 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 5 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 8 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 51 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 2.5 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat, Faeces/Coag -ve staph; H.S./Cl difficile + Toxin; Faeces/Herpes simplex; Mouth |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NONE |
| COMPLICATIONS POST ABMT | : | NIL OF NOTE |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 132 |
| PATIENT NAME | | : Y OLLIVIER |
| HOSPITAL NUMBER | | : FC5586 |
| DATE OF BIRTH | | : 10.8.36 |
| AGE IN YEARS | | : 47 |
| SEX | | : MALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 15.8.83 |
| DATE OF 1ST CR | | : 26.10.83 |
| DATE OF CR PRE-ABMT | | : 26.10.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 10.2.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 20.2.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.5 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 19 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 19 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 24 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 35 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 35 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 15 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 15 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 6 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 6 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 54 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 5.5 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | E coli; Blood, H.S., Faeces/Coag -ve staph; Blood/Cl difficile; Faeces/ diptheroids; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | |
|---|---|
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : NONE |
| COMPLICATIONS POST ABMT | : NIL OF NOTE |
| DATE OF RELAPSE | : 14.1.85 |
| SITE OF RELAPSE | : MEDULLARY |
| DATE OF DEATH | : 16.9.85 |
| CAUSE OF DEATH | : AML |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 135 |
| PATIENT NAME | | : N YOUNIS |
| HOSPITAL NUMBER | | : PP (PORTLAND HOSPITAL) |
| DATE OF BIRTH | | : 13.1.71 |
| AGE IN YEARS | | : 13 |
| SEX | | : F |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : NOT KNOWN |
| DATE OF DIAGNOSIS | | : AUGUST 81 |
| DATE OF 1ST CR | | : NOT KNOWN |
| DATE OF CR PRE-ABMT | | : 30.8.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 2ND CR |
| DATE OF HARVEST | I | : 1.3.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 2ND CR |
| DATE OF ABMT | I | : 10.3.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.5 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 12 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 16 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 22

DAYS UNTIL PLATELETS >100 X $10^9$/L II:

LENGTH OF ADMISSION IN DAYS I : NA

LENGTH OF ADMISSION IN DAYS II:

NO. OF DAYS TEMP. > $37.2^0$C I : NA

NO. OF DAYS TEMP. > $37.2^0$C II:

NO. OF DAYS TEMP. > $38.0^0$C I : NA

NO. OF DAYS TEMP. > $38.0^0$C II:

NO. OF ANTIBIOTICS USED I : NA

NO. OF ANTIBIOTICS USED II:

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II:

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II:

OTHER BLOOD PRODUCTS USED I : NA

OTHER BLOOD PRODUCTS USED II:

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II:

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II:

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Staph aureus; Nose, Throat, H.S./E coli, Proteus mirabilis; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | MAINTENANCE CHEMOTHERAPY |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 143 |
| PATIENT NAME | | : D FIGG |
| HOSPITAL NUMBER | | : FD0170 |
| DATE OF BIRTH | | : 20.9.35 |
| AGE IN YEARS | | : 49 |
| SEX | | : MALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 27.1.84 |
| DATE OF 1ST CR | | : 16.2.84 |
| DATE OF CR PRE-ABMT | | : 16.2.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 13.4.84 |
| DATE OF HARVEST | II | : 27.7.84 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 29.5.84 |
| DATE OF ABMT | II | : 11.8.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.46 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 2.63 |
| GM CFC X $10^4$/KG | I | : 12.54 |
| GM CFC X $10^4$/KG | II | : 15 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 14 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 14 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 20 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 26 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 22 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 27 |
| LENGTH OF ADMISSION IN DAYS | I : 32 |
| LENGTH OF ADMISSION IN DAYS | II: 46 |
| NO. OF DAYS TEMP. >37.2$^0$C | I : 15 |
| NO. OF DAYS TEMP. >37.2$^0$C | II: 14 |
| NO. OF DAYS TEMP. >38.0$^0$C | I : 4 |
| NO. OF DAYS TEMP. >38.0$^0$C | II: 5 |
| NO. OF ANTIBIOTICS USED | I : 8 |
| NO. OF ANTIBIOTICS USED | II: 7 |
| NO. OF UNITS OF BLOOD | I : 6 |
| NO. OF UNITS OF BLOOD | II: 12 |
| NO. OF UNITS OF PLATELETS USED | I : 29 |
| NO. OF UNITS OF PLATELETS USED | II: 104 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: GRANULOCYTES 7 DAYS / PPF |
| WEIGHT LOSS IN KG | I : 5 |
| WEIGHT LOSS IN KG | II: 5 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | INFECTION HICKMAN / TIFFLITIS |
| COMPLICATIONS DURING ABMT | II: | ECTHYMA GANGRENOSUM ON FACE/GRAND MAL FIT |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat, Faeces, H.S./Coag -ve staph, diptheroids; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Pseud aerogenes; Blood, Face/Coag -ve staph, aspergillus; H.S./Staph aureus; Skin/Candida; Faeces, Throat/Proteus mirabilis: Faeces/ Strep mitis; Blood |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | GRAND MAL FIT WHEN ANTI-CONVULSANTS STOPPED |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 147 |
| PATIENT NAME | | : M HOWDEN |
| HOSPITAL NUMBER | | : FD3183 |
| DATE OF BIRTH | | : 3.3.49 |
| AGE IN YEARS | | : 35 |
| SEX | | : MALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M5 |
| DATE OF DIAGNOSIS | | : 14.12.83 |
| DATE OF 1ST CR | | : 6.2.84 |
| DATE OF CR PRE-ABMT | | : 6.2.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 22.6.84 |
| DATE OF HARVEST | II | : 7.9.84 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 30.6.84 |
| DATE OF ABMT | II | : 15.9.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.76 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 2.04 |
| GM CFC X $10^4$/KG | I | : 13.62 |
| GM CFC X $10^4$/KG | II | : 15.04 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 19 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 26 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 21 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 26 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 33 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 45 |

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|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 41 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: 75 |
| LENGTH OF ADMISSION IN DAYS | I : 35 |
| LENGTH OF ADMISSION IN DAYS | II: 43 |
| NO. OF DAYS TEMP. >37.2$^0$C | I : 19 |
| NO. OF DAYS TEMP. >37.2$^0$C | II: 3 |
| NO. OF DAYS TEMP. >38.0$^0$C | I : 12 |
| NO. OF DAYS TEMP. >38.0$^0$C | II: 2 |
| NO. OF ANTIBIOTICS USED | I : 3 |
| NO. OF ANTIBIOTICS USED | II: 4 |
| NO. OF UNITS OF BLOOD | I : 7 |
| NO. OF UNITS OF BLOOD | II: 7 |
| NO. OF UNITS OF PLATELETS USED | I : 47 |
| NO. OF UNITS OF PLATELETS USED | II: 64 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: PPF |
| WEIGHT LOSS IN KG | I : 6.5 |
| WEIGHT LOSS IN KG | II: 4.7 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | INFECTION HICKMAN |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Staph aureus; H.S., H. Tip/Coag -ve staph; Blood, H.S./ E coli; Blood |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Candida; Throat, Faeces/Coag -ve staph, diptheroids; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | SUBCLAVIAN VEIN THROMBOSIS |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 148 |
| PATIENT NAME | | : M WESTON |
| HOSPITAL NUMBER | | : FC3978 |
| DATE OF BIRTH | | : 14.9.57 |
| AGE IN YEARS | | : 26 |
| SEX | | : MALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 23.12.83 |
| DATE OF 1ST CR | | : 31.1.84 |
| DATE OF CR PRE-ABMT | | : 31.1.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 29.6.84 |
| DATE OF HARVEST | II | : 12.10.84 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 9.7.84 |
| DATE OF ABMT | II | : 22.10.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.65 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.54 |
| GM CFC X $10^4$/KG | I | : 9.66 |
| GM CFC X $10^4$/KG | II | : 10.46 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 28 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 24 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 39 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 35 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 39 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 49 |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 45 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: (97-135) |
| LENGTH OF ADMISSION IN DAYS | I : 31 |
| LENGTH OF ADMISSION IN DAYS | II: 38 |
| NO. OF DAYS TEMP. >37.2$^0$C | I : 11 |
| NO. OF DAYS TEMP. >37.2$^0$C | II: 10 |
| NO. OF DAYS TEMP. >38.0$^0$C | I : 9 |
| NO. OF DAYS TEMP. >38.0$^0$C | II: 4 |
| NO. OF ANTIBIOTICS USED | I : 5 |
| NO. OF ANTIBIOTICS USED | II: 6 |
| NO. OF UNITS OF BLOOD | I : 7 |
| NO. OF UNITS OF BLOOD | II: 11 |
| NO. OF UNITS OF PLATELETS USED | I : 59 |
| NO. OF UNITS OF PLATELETS USED | II: 102 |
| OTHER BLOOD PRODUCTS USED | I : GRANULOCYTES 4 DAYS |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : 10 |
| WEIGHT LOSS IN KG | II: 10 |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NO |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | PAIN AT SITE OF HICKMAN |
| COMPLICATIONS DURING ABMT | II: | NIL OF NOTE |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph, diptheroids; H.S./ Flavobacterium; Blood /Candida; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Coag -ve staph; H.S./ Herpes simplex; Mouth /Kleb aerogenes; Blood/Cl difficile Toxin; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | NIL |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 150 |
| PATIENT NAME | | : A SAMAD |
| HOSPITAL NUMBER | | : FD0570 |
| DATE OF BIRTH | | : 10.8.37 |
| AGE IN YEARS | | : 46 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL |
| DATE OF DIAGNOSIS | | : 8.4.84 |
| DATE OF 1ST CR | | : 6.6.84 |
| DATE OF CR PRE-ABMT | | : 6.6.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 5.7.84 |
| DATE OF HARVEST | II | : 7.9.84 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 17.7.84 |
| DATE OF ABMT | II | : 18.9.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.37 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 3.07 |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 15 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 20 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 20 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : NEVER |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 24 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: NEVER |
| LENGTH OF ADMISSION IN DAYS | I : 32 |
| LENGTH OF ADMISSION IN DAYS | II: 31 |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : NA |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: 10 |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : NA |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: 2 |
| NO. OF ANTIBIOTICS USED | I : 3 |
| NO. OF ANTIBIOTICS USED | II: 5 |
| NO. OF UNITS OF BLOOD | I : 6 |
| NO. OF UNITS OF BLOOD | II: 13 |
| NO. OF UNITS OF PLATELETS USED | I : 44 |
| NO. OF UNITS OF PLATELETS USED | II: 111 |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: NONE |
| WEIGHT LOSS IN KG | I : NA |
| WEIGHT LOSS IN KG | II: NIL |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: NA |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | LUNG INFECTION |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida;Throat/Herpes simplex; Mouth/Coag -ve staph; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Candida; Throat, Sputum, Faeces/Haem influenzae; Sputum Coag -ve staph; H.S. |
| STATUS POST ABMT | : | DEAD |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 13.10.84 |
| CAUSE OF DEATH | : | ADULT RESPIRATORY DISTRESS SYNDROME |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 156 |
| PATIENT NAME | | : S MORRIS |
| HOSPITAL NUMBER | | : FC9110 |
| DATE OF BIRTH | | : 1.6.65 |
| AGE IN YEARS | | : 19 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M2 |
| DATE OF DIAGNOSIS | | : AUGUST 83 |
| DATE OF 1ST CR | | : NOVEMBER 83 |
| DATE OF CR PRE-ABMT | | : NOVEMBER 83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 17.8.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 27.8.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.5 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 16 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 22 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 24 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 30 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. >37.2$^0$C | I : 22 |
| NO. OF DAYS TEMP. >37.2$^0$C | II: |
| NO. OF DAYS TEMP. >38.0$^0$C | I : 12 |
| NO. OF DAYS TEMP. >38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 7 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 7 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 80 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 1.4 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph, Staph aureus, diptheroids; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 15.12.85 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 16.1.86 |
| CAUSE OF DEATH | : | AML |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 157 |
| PATIENT NAME | | : S COHEN |
| HOSPITAL NUMBER | | : FC3975 |
| DATE OF BIRTH | | : 5.4.62 |
| AGE IN YEARS | | : 22 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL L2 |
| DATE OF DIAGNOSIS | | : 19.12.83 |
| DATE OF 1ST CR | | : 19.7.84 |
| DATE OF CR PRE-ABMT | | : 19.7.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 31.8.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 10.9.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 3.2 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 20 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 28 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. > 37.2$^0$C | I : 20 |
| NO. OF DAYS TEMP. > 37.2$^0$C | II: |
| NO. OF DAYS TEMP. > 38.0$^0$C | I : 13 |
| NO. OF DAYS TEMP. > 38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 8 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 14 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 104 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : GRANULOCYTES 7 DAYS/PPF & FFP |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : NIL, GAINED 3 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : YES |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | LUNG INFECTION |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S., Sputum/Strep sanguis; Blood |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | DEAD |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 3.10.84 |
| CAUSE OF DEATH | : | ADULT RESPIRATORY DISTRESS SYNDROME |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 160 |
| PATIENT NAME | | : P LANGFORD |
| HOSPITAL NUMBER | | : FD4844 |
| DATE OF BIRTH | | : 16.5.48 |
| AGE IN YEARS | | : 36 |
| SEX | | : MALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M1 |
| DATE OF DIAGNOSIS | | : 23.1.84 |
| DATE OF 1ST CR | | : 23.3.84 |
| DATE OF CR PRE-ABMT | | : 23.3.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 12.10.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 17.10.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.9 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 19 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 21 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 36 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 43 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 40 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. >37.2$^0$C | I : 12 |
| NO. OF DAYS TEMP. >37.2$^0$C | II: |
| NO. OF DAYS TEMP. >38.0$^0$C | I : 9 |
| NO. OF DAYS TEMP. >38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 7 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 5 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 106 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 10.5 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | GRAM -VE SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | E coli; Blood/ Candida; Mouth, Throat/Coag -ve staph, diptheroids; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | TRANSIENT THROMBOCYTOPENIA |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 163 |
| PATIENT NAME | | : R MORRIS |
| HOSPITAL NUMBER | | : FD1336 |
| DATE OF BIRTH | | : 14.2.48 |
| AGE IN YEARS | | : 36 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M4 |
| DATE OF DIAGNOSIS | | : 20.4.84 |
| DATE OF 1ST CR | | : 21.8.84 |
| DATE OF CR PRE-ABMT | | : 21.8.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 19.10.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 29.10.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.65 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 20 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 26 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 29 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : 35 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 32 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. >37.2$^0$C | I : 10 |
| NO. OF DAYS TEMP. >37.2$^0$C | II: |
| NO. OF DAYS TEMP. >38.0$^0$C | I : 3 |
| NO. OF DAYS TEMP. >38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 4 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 6 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 39 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 1 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Mouth, Throat/Coag -ve staph, diptheroids; H.S./Cl difficile Toxin; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | IMPAIRED LEFT VENTRICULAR FUNCTION AS DEMONSTRATED BY A RADIONUCLIDE VENTRICULOGRAM |
| DATE OF RELAPSE | : | 17.6.85 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 18.11.85 |
| CAUSE OF DEATH | : | AML |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 164 |
| PATIENT NAME | | : A PEARSON |
| HOSPITAL NUMBER | | : 329455 |
| DATE OF BIRTH | | : |
| AGE IN YEARS | | : 16 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : L2 |
| DATE OF DIAGNOSIS | | : 20.7.84 |
| DATE OF 1ST CR | | : 17.8.84 |
| DATE OF CR PRE-ABMT | | : 17.8.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 1.11.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 12.11.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.33 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 13 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 23 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 17 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 23

DAYS UNTIL PLATELETS >100 X $10^9$/L II:

LENGTH OF ADMISSION IN DAYS I : NA

LENGTH OF ADMISSION IN DAYS II:

NO. OF DAYS TEMP. > $37.2^0$C I : NA

NO. OF DAYS TEMP. > $37.2^0$C II:

NO. OF DAYS TEMP. > $38.0^0$C I : NA

NO. OF DAYS TEMP. > $38.0^0$C II:

NO. OF ANTIBIOTICS USED I : NA

NO. OF ANTIBIOTICS USED II:

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II:

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II:

OTHER BLOOD PRODUCTS USED I : NA

OTHER BLOOD PRODUCTS USED II:

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II:

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II:

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | PERICARDITIS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat/Coag -ve staph; H tip, Throat, Skin/E. coli; Blood/Strep viridans; Throat |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | MAINTENANCE CHEMOTHERAPY |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 1.10.85 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 174 |
| PATIENT NAME | | : S COOPER |
| HOSPITAL NUMBER | | : FF4822 |
| DATE OF BIRTH | | : 28.5.44 |
| AGE IN YEARS | | : 40 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M2 |
| DATE OF DIAGNOSIS | | : 2.6.84 |
| DATE OF 1ST CR | | : 19.9.84 |
| DATE OF CR PRE-ABMT | | : 19.9.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 11.1.85 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 22.1.85 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.47 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 17 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 31 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 32 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | |
|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: |
| LENGTH OF ADMISSION IN DAYS | I : 49 |
| LENGTH OF ADMISSION IN DAYS | II: |
| NO. OF DAYS TEMP. >37.2$^0$C | I : 8 |
| NO. OF DAYS TEMP. >37.2$^0$C | II: |
| NO. OF DAYS TEMP. >38.0$^0$C | I : 1 |
| NO. OF DAYS TEMP. >38.0$^0$C | II: |
| NO. OF ANTIBIOTICS USED | I : 7 |
| NO. OF ANTIBIOTICS USED | II: |
| NO. OF UNITS OF BLOOD | I : 4 |
| NO. OF UNITS OF BLOOD | II: |
| NO. OF UNITS OF PLATELETS USED | I : 20 |
| NO. OF UNITS OF PLATELETS USED | II: |
| OTHER BLOOD PRODUCTS USED | I : NONE |
| OTHER BLOOD PRODUCTS USED | II: |
| WEIGHT LOSS IN KG | I : 5 |
| WEIGHT LOSS IN KG | II: |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | I : NO |
| TOTAL PARENTERAL NUTRITION ADMINISTERED | II: |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NIL OF NOTE |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S. Cl difficile Toxin; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | |
|---|---|
| STATUS POST ABMT | : RELAPSE |
| TREATMENT POST ABMT | : FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : |
| DATE OF RELAPSE | : 25.2.85 |
| SITE OF RELAPSE | : MEDULLARY |
| DATE OF DEATH | : 8.7.85 |
| CAUSE OF DEATH | : AML |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : B1 |
| PATIENT NAME | | : B BAINS |
| HOSPITAL NUMBER | | : QE HOSPITAL |
| DATE OF BIRTH | | : 9.1.66 |
| AGE IN YEARS | | : 18 |
| SEX | | : M |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL L1 |
| DATE OF DIAGNOSIS | | : 15.1.82 |
| DATE OF 1ST CR | | : 16.3.82 |
| DATE OF CR PRE-ABMT | | : 16.3.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 6.12.83 |
| DATE OF HARVEST | II | : 26.3.84 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 13.12.83 |
| DATE OF ABMT | II | : 9.4.84 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.3 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.0 |
| GM CFC X $10^4$/KG | I | : 7.0 |
| GM CFC X $10^4$/KG | II | : 0.6 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 28 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 24 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 28 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : NEVER |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 42

DAYS UNTIL PLATELETS >100 X $10^9$/L II: NEVER

LENGTH OF ADMISSION IN DAYS I : NA

LENGTH OF ADMISSION IN DAYS II: NA

NO. OF DAYS TEMP. > $37.2^0$C I : NA

NO. OF DAYS TEMP. > $37.2^0$C II: NA

NO. OF DAYS TEMP. > $38.0^0$C I : NA

NO. OF DAYS TEMP. > $38.0^0$C II: NA

NO. OF ANTIBIOTICS USED I : NA

NO. OF ANTIBIOTICS USED II: NA

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II: NA

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II: NA

OTHER BLOOD PRODUCTS USED I : NA

OTHER BLOOD PRODUCTS USED II: NA

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II: NA

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II: NA

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATION |
| COMPLICATIONS DURING ABMT | II: | LUNG INFECTION |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S./ Strep faecalis; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Coag -ve staph; Faeces/Strep faecalis E coli; Faeces Candida; Throat |
| STATUS POST ABMT | : | DEAD |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 7.5.84 |
| CAUSE OF DEATH | : | ADULT RESPIRATORY DISTRESS SYNDROME |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : B2 |
| PATIENT NAME | | : B MELLET |
| HOSPITAL NUMBER | | : QE HOSPITAL |
| DATE OF BIRTH | | : 2.11.33 |
| AGE IN YEARS | | : 49 |
| SEX | | : F |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : cALL L1 |
| DATE OF DIAGNOSIS | | : 4.9.82 |
| DATE OF 1ST CR | | : 9.11.82 |
| DATE OF CR PRE-ABMT | | : 9.11.82 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 30.10.83 |
| DATE OF HARVEST | II | : 21.3.84 |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 16.2.84 |
| DATE OF ABMT | II | : 18.3.85 |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.3 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1.6 |
| GM CFC X $10^4$/KG | I | : 1.1 |
| GM CFC X $10^4$/KG | II | : 2.6 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 11 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 23 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 12 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 23 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 16 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : 34 |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 20

DAYS UNTIL PLATELETS >100 X $10^9$/L II: 40

LENGTH OF ADMISSION IN DAYS I : NA

LENGTH OF ADMISSION IN DAYS II: NA

NO. OF DAYS TEMP. > $37.2^0$C I : NA

NO. OF DAYS TEMP. > $37.2^0$C II: NA

NO. OF DAYS TEMP. > $38.0^0$C I : NA

NO. OF DAYS TEMP. > $38.0^0$C II: NA

NO. OF ANTIBIOTICS USED I : NA

NO. OF ANTIBIOTICS USED II: NA

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II: NA

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II: NA

OTHER BLOOD PRODUCTS USED I : NA

OTHER BLOOD PRODUCTS USED II: NA

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II: NA

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II: NA

| | |
|---|---|
| COMPLICATIONS DURING ABMT | I : NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: ATRIAL TACHYCARDIA |
| POSITIVE MICROBIOLOGY ISOLATES | I : Staph aureus; Blood |
| POSITIVE MICROBIOLOGY ISOLATES | II: Coag -ve staph; Blood, faeces/ Candida; Faeces/ Clostridium sp.; Faeces |
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : |
| COMPLICATIONS POST ABMT | : |
| DATE OF RELAPSE | : |
| SITE OF RELAPSE | : |
| DATE OF DEATH | : |
| CAUSE OF DEATH | : |
| CURRENT STATUS | : WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : B3 |
| PATIENT NAME | | : B WARNER |
| HOSPITAL NUMBER | | : QE HOSPITAL |
| DATE OF BIRTH | | : 16.4.42 |
| AGE IN YEARS | | : 42 |
| SEX | | : MALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M4 |
| DATE OF DIAGNOSIS | | : 17.10.83 |
| DATE OF 1ST CR | | : 26.2.84 |
| DATE OF CR PRE-ABMT | | : 26.2.84 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 13.3.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 20.3.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.5 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : 4.1 |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 11 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 30 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 33 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 40

DAYS UNTIL PLATELETS >100 X $10^9$/L II:

LENGTH OF ADMISSION IN DAYS I : NA

LENGTH OF ADMISSION IN DAYS II:

NO. OF DAYS TEMP. > $37.2^0$C I : NA

NO. OF DAYS TEMP. > $37.2^0$C II:

NO. OF DAYS TEMP. > $38.0^0$C I : NA

NO. OF DAYS TEMP. > $38.0^0$C II:

NO. OF ANTIBIOTICS USED I : NA

NO. OF ANTIBIOTICS USED II:

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II:

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II:

OTHER BLOOD PRODUCTS USED I : NA

OTHER BLOOD PRODUCTS USED II:

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II:

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II:

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | a haem strep; Blood/ Coag -ve staph; H.S., Nose |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 27.5.84 |
| SITE OF RELAPSE | : | CNS |
| DATE OF DEATH | : | 17.6.84 |
| CAUSE OF DEATH | : | AML |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : B4 |
| PATIENT NAME | | : J BLICK |
| HOSPITAL NUMBER | | : QE HOSPITAL |
| DATE OF BIRTH | | : 18.5.27 |
| AGE IN YEARS | | : 55 |
| SEX | | : FEMALE |
| DIAGNOSIS | | : AML |
| CLASSIFICATION | | : M2 |
| DATE OF DIAGNOSIS | | : 30.3.83 |
| DATE OF 1ST CR | | : 10.6.83 |
| DATE OF CR PRE-ABMT | | : 10.6.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 22.11.83 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 1ST CR |
| DATE OF ABMT | I | : 9.4.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.9 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : NA |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 28 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 30 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 49 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : 61

DAYS UNTIL PLATELETS >100 X $10^9$/L II:

LENGTH OF ADMISSION IN DAYS I : NA

LENGTH OF ADMISSION IN DAYS II:

NO. OF DAYS TEMP. >37.2$^0$C I : NA

NO. OF DAYS TEMP. >37.2$^0$C II:

NO. OF DAYS TEMP. >38.0$^0$C I : NA

NO. OF DAYS TEMP. >38.0$^0$C II:

NO. OF ANTIBIOTICS USED I : NA

NO. OF ANTIBIOTICS USED II:

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II:

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II:

OTHER BLOOD PRODUCTS USED I : NA

OTHER BLOOD PRODUCTS USED II:

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II:

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II:

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | HAEMORRHAGIC CYSTITIS & LVF |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph, diptheroids; H.S./ Proteus mirabilis; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 17.10.84 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 6.12.84 |
| CAUSE OF DEATH | : | AML |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : B5 |
| PATIENT NAME | | : S TURNER |
| HOSPITAL NUMBER | | : QE HOSP |
| DATE OF BIRTH | | : 8.9.64 |
| AGE IN YEARS | | : 19 |
| SEX | | : F |
| DIAGNOSIS | | : ALL |
| CLASSIFICATION | | : L2 |
| DATE OF DIAGNOSIS | | : 1.5.79 |
| DATE OF 1ST CR | | : 1.6.79 |
| DATE OF CR PRE-ABMT | | : 10.9.83 |
| STATUS AT TIME OF 1ST HARVEST | | : 3RD CR |
| DATE OF HARVEST | I | : 27.3.84 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : 3RD CR |
| DATE OF ABMT | I | : 9.5.84 |
| DATE OF ABMT | II | : NOT DONE |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.2 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| GM CFC X $10^4$/KG | I | : 2.4 |
| GM CFC X $10^4$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 22 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 42 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : 71 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

DAYS UNTIL PLATELETS >100 X $10^9$/L I : NEVER

DAYS UNTIL PLATELETS >100 X $10^9$/L II:

LENGTH OF ADMISSION IN DAYS I : NA

LENGTH OF ADMISSION IN DAYS II:

NO. OF DAYS TEMP. > $37.2^0$C I : NA

NO. OF DAYS TEMP. > $37.2^0$C II:

NO. OF DAYS TEMP. > $38.0^0$C I : NA

NO. OF DAYS TEMP. > $38.0^0$C II:

NO. OF ANTIBIOTICS USED I : NA

NO. OF ANTIBIOTICS USED II:

NO. OF UNITS OF BLOOD I : NA

NO. OF UNITS OF BLOOD II:

NO. OF UNITS OF PLATELETS USED I : NA

NO. OF UNITS OF PLATELETS USED II:

OTHER BLOOD PRODUCTS USED I : NA

OTHER BLOOD PRODUCTS USED II:

WEIGHT LOSS IN KG I : NA

WEIGHT LOSS IN KG II:

TOTAL PARENTERAL NUTRITION ADMINISTERED I : NA

TOTAL PARENTERAL NUTRITION ADMINISTERED II:

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | COLLAPSE DURING MARROW INFUSION |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | B haem Strep; Blood/ Coag -ve staph; H.S./ E coli; Urine |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | MAINTENANCE CHEMOTHERAPY |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 10.10.84 |
| SITE OF RELAPSE | : | MEDULLARY |
| DATE OF DEATH | : | 8.1.85 |
| CAUSE OF DEATH | : | ALL |
| CURRENT STATUS | : | DEAD |

# APPENDIX II

PATIENT DATA - LYMPHOMA

ABBREVIATIONS

NA, Data not available.

PP, Private patient.

SEX:

M, male; F, female.

DIAGNOSIS:

NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease.

STAGE AT DIAGNOSIS:

This refers to the Ann Arbor staging classification.

CLASSIFICATION:

INT GRADE, Intermediate grade diffuse; HIGH GRADE, High grade diffuse; NS, Nodular sclerosing; MC, Mixed cellularity.

TREATMENT PRE ABMT:

CHOP; Cyclophosphamide, Adriamycin, Vincristine, Prednisolone.

M BACOD; Methotrexate, Bleomycin, Adriamycin, Cyclophosphamide, Vincristine, Dexamethasone.

BACOP; Bleomycin, Adriamycin, Cyclophosphamide, Vincristine, Prednisolone.

M BACOP; Methotrexate, Bleomycin, Adriamycin, Cyclophosphamide, Vincristine, Prednisolone.

HD MTX; High dose methotrexate.

DXT; Radiotherapy.

EVAP; VP16, Vinblastine, Adriamycin, Prednisolone.

Cyt/Thio/Cyclo, Cytosine Arabinoside, Thioguanine, Cyclophosphamide.

IT MTX; Intrathecal methotrexate.

MOPP; Nitrogen Mustard, Vincristine, Procarbazine, Prednisolone.

LOPP; Chlorambucil, Vincristine, Procarbazine, Prednisolone.

Cis Plat; Cis Platinum.

VIND/VP16/CCNU/DEX Vindesine, VP16, Lomustine, Dexamethasone.

ProMACE; Prednisolone, Methotrexate, Adriamycin, Cyclophosphamide, VP16.

COP; Cyclophosphamide, Vincristine, Prednisolone.

CCNU/Bl/Vbl/P; Lomustine (CCNU), Bleomycin, Vinblastine, Prednisolone.

ABVD; Adriamycin, Bleomycin, Vinblastine, Imidazole Carboximide.

AVD; Adriamycin, Vinblastine, Imidazole Carboximide.

HD ARA C; High dose Cytosine Arabinoside.

OPEC; Vincristine, Prednisolone, VP16, Cyclophosphamide.

CCNU/Bleo/Vind; Lomustine, Bleomycin, Vindesine.

C/Vbl/Bl; Cyclophosphamide, Vinblastine, Bleomycin.

STATUS AT TIME OF ABMT:

RR, Resistant Relapse; NON RR, Non Resistant Relapse.

ABMT PROTOCOL USED;

UCH I & II, BEAM, BNLI.

STATUS POST ABMT:

CR, Complete Remission; PR, Partial Remission; NE, Not Evaluable; NR, No Response.

MICROBIOLOGY:

Coag -ve staph, Coagulase negative staphylococci

H.S., Hickman entry site.

Pseud, Pseudomonas

E coli, Escherichia coli

H tip, Hickman tip

a haem strep, a haemolytic streptococcus

B haem strep, B haemolytic streptococcus

Cl, Clostridium

Staph, staphylococcus

sp., species.

Strep, streptococcus

Kleb, klebsiella species

Haem, haemophilus

Myco, mycobacterium

Gp B, Group B

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 34 |
| PATIENT NAME | : | R TURNER |
| HOSPITAL NUMBER | : | EV0794 |
| DATE OF BIRTH | : | 24.6.42 |
| AGE IN YEARS | : | 38 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | III |
| CLASSIFICATION | : | INT GRADE |
| DATE OF DIAGNOSIS | : | 14.5.79 |
| TREATMENT PRE ABMT | : | CHOP |
| | | M BACOD |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF 1ST HARVEST | : | RELAPSE |
| DATE OF HARVEST | I : | 22.6.81 |
| DATE OF HARVEST | II: | 1ST MARROW |
| | | HALVED |
| STATUS AT TIME OF ABMT | I : | RR |
| DATE OF ABMT | I : | 16.9.81 |
| DATE OF ABMT | II: | 22.10.81 |
| ABMT PROTOCOL USED | : | UCH I & II |
| NUCLEATED CELL COUNT X $10^8$/KG | I : | 1.4 |
| NUCLEATED CELL COUNT X $10^8$/KG | II: | NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : | 13 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: | 15 |

| | | |
|---|---|---|
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : | 13 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: | 16 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 14 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | 12 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 30 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | 14 |
| COMPLICATIONS DURING ABMT | I : | SUBCLAVIAN VEIN THROMBOSIS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | NIL |
| POSITIVE MICROBIOLOGY ISOLATES | II: | NIL |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | NIL OF NOTE |
| DATE OF RELAPSE | : | 25.4.82 |
| SITE OF RELAPSE | : | MEDULLARY & ELSEWHERE |
| DATE OF DEATH | : | 14.5.82 |
| CAUSE OF DEATH | : | LEUKAEMIC PHASE OF DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 61 |
| PATIENT NAME | : | R TIFFIN |
| HOSPITAL NUMBER | : | EL8793 |
| DATE OF BIRTH | : | 21.4.27 |
| AGE IN YEARS | : | 55 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | III |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | APRIL 78 |
| TREATMENT PRE ABMT | : | MOPP X 6 |
| | | BACOP X 5 |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 3.8.82 |
| STATUS AT TIME OF ABMT | I : | RR |
| DATE OF ABMT | I : | 8.8.82 |
| DATE OF ABMT | II: | 5.12.82 |
| ABMT PROTOCOL USED | : | UCH I & II |
| NUCLEATED CELL COUNT X $10^8$/KG | : | NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : | 32 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: | 23 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : | 34 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: | 25 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 46 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | 38 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 60 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | 73 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | INFECTION HICKMAN ENTRY SITE: REQUIRED GRANULOCYTES |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Mouth,faeces /Coag -ve staph, Diphtheroids, Strep faecalis; H.S. |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Candida; Throat, faeces/Staph aureus, B haem strep; Throat /Kleb aerogenes; Blood, urine, faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NONE |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 6.4.83 |
| CAUSE OF DEATH | : | CARDIAC FAILURE IN CR |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 65 |
| PATIENT NAME | | : C HEPBURN |
| HOSPITAL NUMBER | | : EX6032 |
| DATE OF BIRTH | | : 30.12.43 |
| AGE IN YEARS | | : 39 |
| SEX | | : M |
| DIAGNOSIS | | : NHL |
| STAGE AT DIAGNOSIS | | : IV |
| CLASSIFICATION | | : INT GRADE |
| DATE OF DIAGNOSIS | | : 15.9.81 |
| TREATMENT PRE ABMT | | : CHOP X 7 |
| | | BACOP |
| | | M BACOP |
| PREVIOUS MARROW INFILTRATION | | : NO |
| STATUS AT TIME OF 1ST HARVEST | | : RELAPSE |
| DATE OF HARVEST | I | : 5.7.82 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : RR |
| DATE OF ABMT | I | : 12.7.82 |
| DATE OF ABMT | II | : 12.9.82 |
| ABMT PROTOCOL USED | | : UCH I & II |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 11 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 17 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 20 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 20 |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 21 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | 16 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 25 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | 19 |
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; H.S., Throat/ Diptheroids; H.S./ Candida; Throat, Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Candida; Mouth/ Pseud aerogenes; Rectal |

| | | |
|---|---|---|
| STATUS POST ABMT | : | PR |
| TREATMENT POST ABMT | : | DXT TO RESIDUAL ABDOMINAL MASS |
| COMPLICATIONS POST ABMT | : | NIL OF NOTE |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 75 |
| PATIENT NAME | : | S SAUNDERS |
| HOSPITAL NUMBER | : | FA0650 |
| DATE OF BIRTH | : | 3.5.23 |
| AGE IN YEARS | : | 49 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IIB |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | DECEMBER 81 |
| TREATMENT PRE ABMT | : | CHOP |
| | | HD MTX |
| | | DXT |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF 1ST HARVEST | : | RELAPSE |
| DATE OF HARVEST | I : | 8.11.82 |
| DATE OF HARVEST | II: | NOT DONE |
| STATUS AT TIME OF ABMT | I : | RR |
| DATE OF ABMT | I : | 14.11.82 |
| DATE OF ABMT | II: | NOT DONE |
| ABMT PROTOCOL USED | : | UCH I |
| NUCLEATED CELL COUNT X $10^8$/KG | I : | 1.35/2 |
| NUCLEATED CELL COUNT X $10^8$/KG | II: | |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : | NEVER |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: | |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : | NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: | |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |
| COMPLICATIONS DURING ABMT | I : | SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat, faeces/Staph aureus; H.S./E coli,Citrobacter freundii; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | NE |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 23.11.82 |
| CAUSE OF DEATH | : | SEPTICAEMIA |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 88 |
| PATIENT NAME | : | M SMITHERS |
| HOSPITAL NUMBER | : | GUY'S HOSPITAL |
| DATE OF BIRTH | : | 4.7.55 |
| AGE IN YEARS | : | 28 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIB |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | 26.3.79 |
| TREATMENT PRE ABMT | : | MOPP X 6 |
| | | CCNU/BL/VBL/P |
| | | DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 14.2.83 |
| STATUS AT TIME OF ABMT | I : | RR |
| DATE OF ABMT | I : | 22.2.83 |
| DATE OF ABMT | II: | 24.4.83 |
| ABMT PROTOCOL USED | : | UCH I & II |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.2 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : | 13 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: | 15 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : | 23 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: | 16 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 17 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | 16 |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 28 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | 24 |
| COMPLICATIONS DURING ABMT | I : | HAEMORRHAGIC CYSTITIS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATION |
| POSITIVE MICROBIOLOGY ISOLATES | I : | |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 15.7.83 |
| SITE OF RELAPSE | : | RETURN OF B SYMPTOMS |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 94 |
| PATIENT NAME | | : R LEGGETT |
| HOSPITAL NUMBER | | : MIDDLESEX HOSPITAL |
| DATE OF BIRTH | | : 25.2.33 |
| AGE IN YEARS | | : 50 |
| SEX | | : M |
| DIAGNOSIS | | : NHL |
| STAGE AT DIAGNOSIS | | : II |
| CLASSIFICATION | | : INT GRADE |
| DATE OF DIAGNOSIS | | : JULY 81 |
| TREATMENT PRE ABMT | | : ORCHIDECTOMY CHOP X 6 |
| PREVIOUS MARROW INFILTRATION | | : NO |
| STATUS AT TIME OF 1ST HARVEST | | : 1ST CR |
| DATE OF HARVEST | I | : 10.9.81 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : NON RR |
| DATE OF ABMT | I | : 6.4.83 |
| DATE OF ABMT | II | : NOT DONE |
| ABMT PROTOCOL USED | | : UCH I |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 2.4 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 16 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 19 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 15 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 16 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Acinetobacter sp; Blood/E coli; H. tip/B haem strep; Throat |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 6.1.84 |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 16.2.84 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 99 |
| PATIENT NAME | | : R MOLYNEUX |
| HOSPITAL NUMBER | | : MIDDLESEX HOSPITAL |
| DATE OF BIRTH | | : 5.6.45 |
| AGE IN YEARS | | : 37 |
| SEX | | : M |
| DIAGNOSIS | | : HD |
| STAGE AT DIAGNOSIS | | : IA |
| CLASSIFICATION | | : NS |
| DATE OF DIAGNOSIS | | : 2.9.77 |
| TREATMENT PRE ABMT | | : LOPP |
| | | ABVD |
| | | DXT X 2 |
| PREVIOUS MARROW INFILTRATION | | : NO |
| STATUS AT TIME OF HARVEST | | : RELAPSE |
| DATE OF HARVEST | | : 17.2.83 |
| STATUS AT TIME OF ABMT | I | : RR |
| DATE OF ABMT | I | : 17.2.83 |
| DATE OF ABMT | II | : NOT DONE |
| ABMT PROTOCOL USED | | : UCH I |
| NUCLEATED CELL COUNT X $10^8$/KG | | : 1.5 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : NEVER |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I | : NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II | : |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |
| COMPLICATIONS DURING ABMT | I : | SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Acinetobacter sp; Blood |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | NE |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 3.3.83 |
| CAUSE OF DEATH | : | ACINETOBACTER SEPTICAEMIA |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 101 |
| PATIENT NAME | | : I SHIPLEY |
| HOSPITAL NUMBER | | : ES3810 |
| DATE OF BIRTH | | : 24.4.36 |
| AGE IN YEARS | | : 47 |
| SEX | | : M |
| DIAGNOSIS | | : NHL |
| STAGE AT DIAGNOSIS | | : CONJUNCTIVAL |
| CLASSIFICATION | | : INT GRADE |
| DATE OF DIAGNOSIS | | : JULY 79 |
| TREATMENT PRE ABMT | | : CHOP X 6 |
| | | DXT |
| PREVIOUS MARROW INFILTRATION | | : NO |
| STATUS AT TIME OF 1ST HARVEST | | : RELAPSE |
| DATE OF HARVEST | I | : 20.5.83 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : NON RR |
| DATE OF ABMT | I | : 28.5.83 |
| DATE OF ABMT | II | : 23.7.83 |
| ABMT PROTOCOL USED | | : UCH I & II |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 1.48/2 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : 1ST MARROW |
| | | HALVED |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 18 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 20 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : 24 |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 15 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | 11 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 17 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | 16 |
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat, Faeces/Staph aureus; H.S./Cl difficile; Faeces |
| POSITIVE MICROBIOLOGY ISOLATES | II: | Candida; Throat/ E coli; Faeces |

| | | |
|---|---|---|
| STATUS POST ABMT | : | PR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 20.2.84 |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |

| | | |
|---|---|---|
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | | : 102 |
| PATIENT NAME | | : L WARD |
| HOSPITAL NUMBER | | : FB2321 |
| DATE OF BIRTH | | : 22.3.55 |
| AGE IN YEARS | | : 28 |
| SEX | | : F |
| DIAGNOSIS | | : NHL |
| STAGE AT DIAGNOSIS | | : IV |
| CLASSIFICATION | | : INT GRADE |
| DATE OF DIAGNOSIS | | : AUGUST 82 |
| TREATMENT PRE ABMT | | : CHOP X 3 |
| | | HD MTX X 4 |
| | | DXT |
| PREVIOUS MARROW INFILTRATION | | : NO |
| STATUS AT TIME OF 1ST HARVEST | | : RELAPSE |
| DATE OF HARVEST | I | : 18.5.83 |
| DATE OF HARVEST | II | : NOT DONE |
| STATUS AT TIME OF ABMT | I | : RR |
| DATE OF ABMT | I | : 7.6.83 |
| DATE OF ABMT | II | : NOT DONE |
| ABMT PROTOCOL USED | | : UCH I |
| NUCLEATED CELL COUNT X $10^8$/KG | I | : 0.72/2 |
| NUCLEATED CELL COUNT X $10^8$/KG | II | : |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I | : 13 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II | : |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I | : 15 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II | : |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 14 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 20 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Candida; Throat, Faeces, vagina/ Coag -ve staph; H.S./E coli; Urine Cl difficile; Faeces / Staph aureus; Nose |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | NR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 17.7.83 |
| SITE OF RELAPSE | : | SKIN, MEDULLARY & ELSEWHERE |
| DATE OF DEATH | : | 8.9.83 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 113 |
| PATIENT NAME | : | K WHITE |
| HOSPITAL NUMBER | : | GUY'S HOSPITAL |
| DATE OF BIRTH | : | 2.10.37 |
| AGE IN YEARS | : | 46 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIIB |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | JUNE 82 |
| TREATMENT PRE ABMT | : | MOPP X 3 |
| | | AVD X 3 |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 29.7.83 |
| STATUS AT TIME OF ABMT | I : | RR |
| DATE OF ABMT | I : | 10.9.83 |
| DATE OF ABMT | II: | NOT DONE |
| ABMT PROTOCOL USED | : | UCH I |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.3 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : | 21 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: | |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : | 21 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 25 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 28 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | BREAKDOWN OF PREVIOUS SKIN GRAFT |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Coag -ve staph; Blood |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NONE |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 114 |
| PATIENT NAME | : | F CAVALLARO |
| HOSPITAL NUMBER | : | 302820 |
| DATE OF BIRTH | : | 25.7.54 |
| AGE IN YEARS | : | 29 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | MESENTERIC MASS (>10cms) ? IIB |
| CLASSIFICATION | : | INT GRADE |
| DATE OF DIAGNOSIS | : | MARCH 83 |
| TREATMENT PRE ABMT | : | CHOP X 4<br>EVAP X 1 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF 1ST HARVEST | : | RELAPSE |
| DATE OF HARVEST | I : | 29.4.83 |
| DATE OF HARVEST | II: | NOT DONE |
| STATUS AT TIME OF ABMT | I : | RR |
| DATE OF ABMT | I : | 16.9.83 |
| DATE OF ABMT | II: | NOT DONE |
| ABMT PROTOCOL USED | : | UCH I |
| NUCLEATED CELL COUNT X $10^8$/KG | I : | NA |
| NUCLEATED CELL COUNT X $10^8$/KG | II: | |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : | 17 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: | |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : | 17 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: | |

| | | |
|---|---|---|
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | 26 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | 33 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |
| COMPLICATIONS DURING ABMT | I : | NO MAJOR COMPLICATIONS |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | NA |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |

| | | |
|---|---|---|
| STATUS POST ABMT | : | NR |
| TREATMENT POST ABMT | : | DXT |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 30.10.83 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 116 |
| PATIENT NAME | : | A TAYLOR |
| HOSPITAL NUMBER | : | GUY'S HOSPITAL |
| DATE OF BIRTH | : | 4.11.59 |
| AGE IN YEARS | : | 24 |
| SEX | : | F |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIAS |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | DECEMBER 81 |
| TREATMENT PRE ABMT | : | MOPP X 3 |
| | | CCNU/BL/VBL/P X 6 |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 11.8.83 |
| STATUS AT TIME OF ABMT | I : | RR |
| DATE OF ABMT | I : | 1.10.83 |
| DATE OF ABMT | II: | NOT DONE |
| ABMT PROTOCOL USED | : | UCH I |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.7/2 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | I : | NEVER |
| DAYS UNTIL WBC >1.0 X $10^9$/L | II: | |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | I : | NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | I : | NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | II: | |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | I : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | II: | |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | I : | SEPTICAEMIA |
| COMPLICATIONS DURING ABMT | II: | |
| POSITIVE MICROBIOLOGY ISOLATES | I : | Staph aureus; Blood |
| POSITIVE MICROBIOLOGY ISOLATES | II: | |
| STATUS POST ABMT | : | CR (AT POST MORTEM NECROTIC TUMOUR ONLY) |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 10.11.83 |
| CAUSE OF DEATH | : | STAPH AUREUS SEPTICAEMIA |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 124 |
| PATIENT NAME | : | P STAPLETON |
| HOSPITAL NUMBER | : | FC0782 |
| DATE OF BIRTH | : | 15.8.54 |
| AGE IN YEARS | : | 29 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IB |
| CLASSIFICATION | : | ATYPICAL |
| DATE OF DIAGNOSIS | : | APRIL 83 |
| TREATMENT PRE ABMT | : | CHOP X 1 |
| | | HD ARA C X 1 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 11.11.83 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 20.11.83 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 0.7 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | NEVER |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | ASPERGILLUS PNEUMONIA |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat, Faeces/Coag -ve staph, diphtheroids; H.S./E. coli, Cl difficile; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 10.1.84 |
| CAUSE OF DEATH | : | ASPERGILLUS PNEUMONIA |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 126 |
| PATIENT NAME | : | I SMITH |
| HOSPITAL NUMBER | : | FA7509 |
| DATE OF BIRTH | : | 5.8.62 |
| AGE IN YEARS | : | 21 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | MEDIASTINAL MASS |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | FEBRUARY 83 |
| TREATMENT PRE ABMT | : | CHOP X 4 |
| | | CYT/THIO/CYCLO |
| | | X 1 |
| | | IT MTX |
| | | DXT |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | PR |
| DATE OF HARVEST | : | 26.6.83 |
| STATUS AT TIME OF ABMT | : | PR |
| DATE OF ABMT | : | 14.12.83 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.4 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 13 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 15 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 15 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 28 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat/Pseud aeruginosa; Faeces/ Staph aureus; H.S., urine/Coag -ve staph; H.S./Acinetobacter sp; Blood |
| STATUS POST ABMT | : | PR |
| TREATMENT POST ABMT | : | DXT TO RESIDUAL MEDIASTINAL MASS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 133 |
| PATIENT NAME | : | T HAIGH |
| HOSPITAL NUMBER | : | GUY'S HOSPITAL |
| DATE OF BIRTH | : | 4.3.43 |
| AGE IN YEARS | : | 41 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | II |
| CLASSIFICATION | : | INT GRADE |
| DATE OF DIAGNOSIS | : | NOVEMBER 83 |
| TREATMENT PRE ABMT | : | CHOP X 2 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 10.2.84 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 22.2.84 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.26 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 20 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 34 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 54 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | SEPTICAEMIA |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat/ Herpes simplex; Mouth |
| STATUS POST ABMT | : | NR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 18.5.84 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 136 |
| PATIENT NAME | : | C INGLE |
| HOSPITAL NUMBER | : | FB0573 |
| DATE OF BIRTH | : | 2.12.65 |
| AGE IN YEARS | : | 19 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | I |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | MAY 83 |
| TREATMENT PRE ABMT | : | M BACOD X 4 DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 2.3.84 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 13.3.84 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.3 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 20 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 28 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 36 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 36 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | SEPTICAEMIA / PERICARDIAL EFFUSION |
| POSITIVE MICROBIOLOGY ISOLATES | : | E coli; Blood/ Candida; Throat/ Coag -ve staph; H.S. |
| STATUS POST ABMT | : | NR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 2.5.84 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 137 |
| PATIENT NAME | : | J VERNON |
| HOSPITAL NUMBER | : | GUY'S HOSPITAL |
| DATE OF BIRTH | : | 17.5.38 |
| AGE IN YEARS | : | 45 |
| SEX | : | F |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | I |
| CLASSIFICATION | : | INT GRADE |
| DATE OF DIAGNOSIS | : | JUNE 80 |
| TREATMENT PRE ABMT | : | CHOP X 6 |
| | | M BACOD X 4 |
| | | DXT X 2 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 2.3.84 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 21.3.84 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.3 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 15 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 17 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 19 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 23 |

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|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Strep; Blood/ Candida; Throat |
| STATUS POST ABMT | : | NR |
| TREATMENT POST ABMT | : | STEROIDS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 28.5.84 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 146 |
| PATIENT NAME | : | D GOODMAN |
| HOSPITAL NUMBER | : | FD1621 |
| DATE OF BIRTH | : | 12.2.59 |
| AGE IN YEARS | : | 25 |
| SEX | : | F |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIA |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | APRIL 82 |
| TREATMENT PRE ABMT | : | LOPP X 6 |
| | | EVAP X 7 |
| | | DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | DIAGNOSIS |
| DATE OF HARVEST | : | 13.5.82 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 1.6.84 |
| ABMT PROTOCOL USED | : | TBI 875 |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 0.85 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 26 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 28 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 26 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 40 |

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|---|---|
| COMPLICATIONS DURING ABMT | : BILATERAL PLEURAL EFFUSIONS TAPPED |
| POSITIVE MICROBIOLOGY ISOLATES | : Candida; Throat, Faeces/Staph aureus; Nose/ E. coli; Faeces |
| STATUS POST ABMT | : PR |
| TREATMENT POST ABMT | : STEROIDS |
| COMPLICATIONS POST ABMT | : PNEUMONITIS |
| DATE OF RELAPSE | : |
| SITE OF RELAPSE | : |
| DATE OF DEATH | : 6.9.84 |
| CAUSE OF DEATH | : RAPIDLY PROGRESSIVE LYMPHOMA |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 153 |
| PATIENT NAME | : | J HINCHLIFFE |
| HOSPITAL NUMBER | : | FD1622 |
| DATE OF BIRTH | : | 28.3.50 |
| AGE IN YEARS | : | 33 |
| SEX | : | F |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IV |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | 4.7.83 |
| TREATMENT PRE ABMT | : | CHOP X 6 |
| | | CIS PLAT X 1 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | 2ND CR |
| DATE OF HARVEST | : | 20.7.84 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 28.7.84 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.04 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 12 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 18 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 24 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 26 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Klebsiella oxytocum: Urine |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 24.9.84 |
| SITE OF RELAPSE | : | NODAL |
| DATE OF DEATH | : | 20.3.85 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 155 |
| PATIENT NAME | : | S PANATTI |
| HOSPITAL NUMBER | : | EY2746 |
| DATE OF BIRTH | : | 14.4.54 |
| AGE IN YEARS | : | 30 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIA |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | 9.12.81 |
| TREATMENT PRE ABMT | : | BACOP/OPEC X 3<br>DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 17.8.84 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 26.8.84 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 3.3 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 11 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 15 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 13 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 24 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Faeces/ Coag -ve staph, diphtheroids; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | HERPES ZOSTER DECEMBER 1985 |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 158 |
| PATIENT NAME | : | E OSBORNE |
| HOSPITAL NUMBER | : | 319422 |
| DATE OF BIRTH | : | 28.11.34 |
| AGE IN YEARS | : | 50 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IVA |
| CLASSIFICATION | : | INT GRADE |
| DATE OF DIAGNOSIS | : | 14.11.83 |
| TREATMENT PRE ABMT | : | CHOP X 6 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 30.8.84 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 10.9.84 |
| ABMT PROTOCOL USED | : | BNLI |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.78 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 16 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 16 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 38 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 46 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | GRAM -VE SEPTICAEMIA |
| POSITIVE MICROBIOLOGY ISOLATES | : | Coag -ve staph, Strep viridans, Bacillus sp, Acinetobacter sp; Blood/coliforms, Kleb sp; Sputum / Candida; Throat |
| STATUS POST ABMT | : | PR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | ? CNS DISEASE<br>? PNEUMOCYSTIS CARINII PNEUMONIA |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 31.3.85 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 161 |
| PATIENT NAME | : | W KENNY |
| HOSPITAL NUMBER | : | 332967 |
| DATE OF BIRTH | : | 30.5.38 |
| AGE IN YEARS | : | 47 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | PRIMARY JEJUNUM |
| CLASSIFICATION | : | INT GRADE |
| DATE OF DIAGNOSIS | : | MARCH 84 |
| TREATMENT PRE ABMT | : | CHOP X 4 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 8.10.84 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 20.10.84 |
| ABMT PROTOCOL USED | : | BNLI |
| NUCLEATED CELL COUNT X $10^8$/KG | : | NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | NEVER |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | OVERWHELMING INFECTION |
| POSITIVE MICROBIOLOGY ISOLATES | : | Staph aureus, Coag -ve staph, Bacillus sp, Strep pneumoniae;Blood /Candida, coliforms, Staph aureus, Coag -ve staph, Haem para-influenzae; Sputum |
| STATUS POST ABMT | : | NE |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 4.11.84 |
| CAUSE OF DEATH | : | CVA, BRONCHOPNEUMONIA |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 166 |
| PATIENT NAME | : | P MOORE |
| HOSPITAL NUMBER | : | 333431 |
| DATE OF BIRTH | : | 1.8.63 |
| AGE IN YEARS | : | 21 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IV |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | 16.3.84 |
| TREATMENT PRE ABMT | : | LOPP X 3 |
| | | EVAP X 1 |
| | | VIND/VP16/CCNU/ |
| | | DEX |
| | | DXT X 2 |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 15.11.84 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 27.11.84 |
| ABMT PROTOCOL USED | : | BNLI |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.69 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | NEVER |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | |
| POSITIVE MICROBIOLOGY ISOLATES | : | Staph aureus; Sputum, Nose/ Coag -ve staph; H.S./ Strep viridans; Throat |
| STATUS POST ABMT | : | NE |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 29.11.84 |
| CAUSE OF DEATH | : | ? TRACHEAL OBSTRUCTION BY TUMOUR |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 168 |
| PATIENT NAME | : | I BEARMAN |
| HOSPITAL NUMBER | : | 316714 |
| DATE OF BIRTH | : | 31.3.29 |
| AGE IN YEARS | : | 56 |
| SEX | : | F |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IVA |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | SEPTEMBER 83 |
| TREATMENT PRE ABMT | : | CHOP X 7 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 29.11.84 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 6.12.84 |
| ABMT PROTOCOL USED | : | BNLI |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.31 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | NEVER |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | NEVER |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | |
| POSITIVE MICROBIOLOGY ISOLATES | : | Pseud aeruginosa; Urine/ Proteus sp; Sputum |
| STATUS POST ABMT | : | NE |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 11.12.84 |
| CAUSE OF DEATH | : | CARDIAC INFILTRATION |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 170 |
| PATIENT NAME | : | D CARNEY |
| HOSPITAL NUMBER | : | FF2941 |
| DATE OF BIRTH | : | 24.3.54 |
| AGE IN YEARS | : | 30 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIIB |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | MARCH 83 |
| TREATMENT PRE ABMT | : | LOPP X 3<br>CCNU/BLEO/VIND<br>X 9 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 6.12.84 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 14.12.84 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.34 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 31 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 31 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 42 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 56 |

| | |
|---|---|
| COMPLICATIONS DURING ABMT | : NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : Candida; Throat, faeces/Coag -ve staph; Blood, H. tip /Kleb aerogenes; Throat/ Mycobacterium xenopi, Candida; Bronchial aspirate |
| STATUS POST ABMT | : CR |
| TREATMENT POST ABMT | : FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : HERPES ZOSTER DECEMBER 1985 |
| DATE OF RELAPSE | : ? AUGUST 85 |
| SITE OF RELAPSE | : NODAL AS BEFORE |
| DATE OF DEATH | : 3.4.86 |
| CAUSE OF DEATH | : SEPSIS |
| CURRENT STATUS | : DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 171 |
| PATIENT NAME | : | A HARRISON |
| HOSPITAL NUMBER | : | GUY'S HOSPITAL |
| DATE OF BIRTH | : | 16.4.59 |
| AGE IN YEARS | : | 25 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIB |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | AUGUST 81 |
| TREATMENT PRE ABMT | : | MOPP X 9 |
| | | EVAP X 8 |
| | | DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | AUGUST 84 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 18.12.84 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.78 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 17 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 23 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 31 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 49 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | GOUTY ARTHRITIS, MUCOSITIS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Coag -ve staph; Blood |
| STATUS POST ABMT | : | PR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 21.7.85 |
| CAUSE OF DEATH | : | RAPIDLY PROGRESSIVE LYMPHOMA |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 177 |
| PATIENT NAME | : | T PACKARD |
| HOSPITAL NUMBER | : | FF2577 |
| DATE OF BIRTH | : | 22.7.48 |
| AGE IN YEARS | : | 36 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIIAS |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | OCTOBER 79 |
| TREATMENT PRE ABMT | : | LOPP X 3 |
| | | MOPP X 4 |
| | | LOPP/EVAP X 2 |
| | | 1/2 MOPP/EVAP |
| | | DXT |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 25.1.85 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 13.2.85 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.75 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 24 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 32 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 57 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 57 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat, faeces/ Coag -ve staph; Blood, H.S. H.tip/ Diphtheroids; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | HEMI BODY IRRADIATION |
| COMPLICATIONS POST ABMT | : | SEPTICAEMIA MAY 1985 |
| DATE OF RELAPSE | : | 15.5.85 |
| SITE OF RELAPSE | : | NODAL AS BEFORE & LUNG INFILTRATES |
| DATE OF DEATH | : | 7.11.85 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 180 |
| PATIENT NAME | : | G GILHAM |
| HOSPITAL NUMBER | : | FF7301 |
| DATE OF BIRTH | : | 30.8.59 |
| AGE IN YEARS | : | 25 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IVB |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | FEBRUARY 83 |
| TREATMENT PRE ABMT | : | MOPP X 6 |
| | | LOPP X 3 |
| | | EVAP X 5 |
| | | CCNU/BLEO/VIND |
| | | DXT |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 15.2.85 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 15.3.85 |
| ABMT PROTOCOL USED | : | TBI 800 |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.96 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 10 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 22 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | NEVER |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | NEVER |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat, bronchial aspirate, sputum, faeces/ Coag -ve staph; H.S., Chest lesion/ Strep pneumoniae; Sputum |
| STATUS POST ABMT | : | PR |
| TREATMENT POST ABMT | : | DXT |
| COMPLICATIONS POST ABMT | : | HERPES ZOSTER JUNE 85 |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | 17.8.85 |
| CAUSE OF DEATH | : | SEPTICAEMIC NO POST MORTEM |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 183 |
| PATIENT NAME | : | J CAPON |
| HOSPITAL NUMBER | : | FH5335 |
| DATE OF BIRTH | : | 7.5.46 |
| AGE IN YEARS | : | 39 |
| SEX | : | F |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IV |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | JULY 84 |
| TREATMENT PRE ABMT | : | CHOP X 6 |
| | | DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | YES |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 26.4.85 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 7.5.85 |
| ABMT PROTOCOL USED | : | BNLI |
| NUCLEATED CELL COUNT X $10^8$/KG | : | NA |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 26 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 29 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 28 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 30 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Bacteroides fragilis; Urine/Candida; Throat, H.S./Diphtheroids, Coag -ve staph, Agrobacterium radiobacter; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | DXT |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 2.9.85 |
| SITE OF RELAPSE | : | EXTRAMEDULLARY - LUMP ON CRANIUM |
| DATE OF DEATH | : | 7.12.85 |
| CAUSE OF DEATH | : | DISEASE |
| CURRENT STATUS | : | DEAD |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 185 |
| PATIENT NAME | : | G MANSER |
| HOSPITAL NUMBER | : | FC7326 |
| DATE OF BIRTH | : | 11.10.71 |
| AGE IN YEARS | : | 13 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IVB |
| CLASSIFICATION | : | MC |
| DATE OF DIAGNOSIS | : | 4.2.84 |
| TREATMENT PRE ABMT | : | BACOP/OPEC X 4 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 1.6.85 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 14.6.85 |
| ABMT PROTOCOL USED | : | TBI & CYCLO |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 14.6/wt |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 13 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 13 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 18 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 22 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat/Strep faecalis; Urine/Strep Gp B; Blood/Staph aureus; Nose, elbow/ Pseud acidovorus: H. tip |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | CHLORAMBUCIL/ PROCARBAZINE/ PREDNISOLONE |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 12.9.85 |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 186 |
| PATIENT NAME | : | S SOUTHBY |
| HOSPITAL NUMBER | : | 314876 |
| DATE OF BIRTH | : | 1.10.62 |
| AGE IN YEARS | : | 23 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IIB |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | 25.10.83 |
| TREATMENT PRE ABMT | : | LOPP X 6 |
| | | EVAP X 3 |
| | | C/Vbl/Bl X 1 |
| | | DXT X 2 |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 6.6.85 |
| STATUS AT TIME OF ABMT | : | RR |
| DATE OF ABMT | : | 17.6.85 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.08 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 25 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 29 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 43 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 52 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Coag -ve staph; Blood/Strep viridans; Sputum/Bacteroides sp; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | HERPES ZOSTER NOVEMBER 85: PNEUMOCYSTIS CARINII OCTOBER 85 |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 187 |
| PATIENT NAME | : | A PAVLOU |
| HOSPITAL NUMBER | : | PP |
| DATE OF BIRTH | : | 23.7.35 |
| AGE IN YEARS | : | 50 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | III |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | OCTOBER 83 |
| TREATMENT PRE ABMT | : | ProMACE/MOPP |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 9.6.85 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 20.6.85 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.73 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 12 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 21 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 16 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 25 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | SEVERE GENERALISED SKIN RASH |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat, faeces/Coag -ve staph; H.S./Pseud aeruginosa; Faeces |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 188 |
| PATIENT NAME | : | R MARSH |
| HOSPITAL NUMBER | : | 320623 |
| DATE OF BIRTH | : | 27.10.55 |
| AGE IN YEARS | : | 30 |
| SEX | : | M |
| DIAGNOSIS | : | HD |
| STAGE AT DIAGNOSIS | : | IVB |
| CLASSIFICATION | : | NS |
| DATE OF DIAGNOSIS | : | JANUARY 84 |
| TREATMENT PRE ABMT | : | LOPP X 9 |
| | | DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 28.6.85 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 5.7.85 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.48 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 22 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 24 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 28 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 32 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | ? FUNGAL PNEUMONIA |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Sputum, faeces/E coli; Urine/ Coag -ve staph; Blood /Herpes simplex;Mouth / ? Fungi x 3; Sputum |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | NIL |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 191 |
| PATIENT NAME | : | M DEBLANK |
| HOSPITAL NUMBER | : | 336160 |
| DATE OF BIRTH | : | 16.3.55 |
| AGE IN YEARS | : | 30 |
| SEX | : | F |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IV |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | NOVEMBER 84 |
| TREATMENT PRE ABMT | : | CHOP X 6 |
| | | DXT |

| | | |
|---|---|---|
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | RELAPSE |
| DATE OF HARVEST | : | 11.7.85 |
| STATUS AT TIME OF ABMT | : | NON RR |
| DATE OF ABMT | : | 20.7.85 |
| ABMT PROTOCOL USED | : | BNLI |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.125 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 13 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 16 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 16 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 17 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | NO MAJOR COMPLICATIONS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat, faeces/Pseud aeruginosa, coliforms; Faeces/a haem strep, neisseria; Throat |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 195 |
| PATIENT NAME | : | N REILLY |
| HOSPITAL NUMBER | : | FF8953 |
| DATE OF BIRTH | : | 5.9.40 |
| AGE IN YEARS | : | 45 |
| SEX | : | F |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | IVA |
| CLASSIFICATION | : | INT GRADE |
| DATE OF DIAGNOSIS | : | MARCH 83 |
| TREATMENT PRE ABMT | : | COP X 4 |
| | | M BACOD X 4 |
| | | DXT |
| PREVIOUS MARROW INFILTRATION | : | YES |
| STATUS AT TIME OF HARVEST | : | 3RD CR |
| DATE OF HARVEST | : | 26.7.85 |
| STATUS AT TIME OF ABMT | : | 3RD CR |
| DATE OF ABMT | : | 13.8.85 |
| ABMT PROTOCOL USED | : | BEAM |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 2.7 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 14 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 15 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 36 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 36 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | SEVERE MUCOSITIS |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat, faeces/Coag -ve staph; H.S. |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | |
| SITE OF RELAPSE | : | |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

| | | |
|---|---|---|
| UNIQUE PATIENT NUMBER | : | 196 |
| PATIENT NAME | : | E CARROLL |
| HOSPITAL NUMBER | : | FC8998 |
| DATE OF BIRTH | : | 6.12.28 |
| AGE IN YEARS | : | 67 |
| SEX | : | M |
| DIAGNOSIS | : | NHL |
| STAGE AT DIAGNOSIS | : | II + CNS |
| CLASSIFICATION | : | HIGH GRADE |
| DATE OF DIAGNOSIS | : | 20.3.84 |
| TREATMENT PRE ABMT | : | M BACOD X 6 |
| | | CRANIO-SPINAL |
| | | DXT |
| | | IT MTX |
| PREVIOUS MARROW INFILTRATION | : | NO |
| STATUS AT TIME OF HARVEST | : | 1ST CR |
| DATE OF HARVEST | : | 31.8.84 |
| STATUS AT TIME OF ABMT | : | 1ST CR |
| DATE OF ABMT | : | 16.8.85 |
| ABMT PROTOCOL USED | : | TBI & CYCLO |
| NUCLEATED CELL COUNT X $10^8$/KG | : | 1.67 |
| DAYS UNTIL WBC >1.0 X $10^9$/L | : | 12 |
| DAYS UNTIL NEUTS >0.5 X $10^9$/L | : | 13 |
| DAYS UNTIL PLATELETS >50 X $10^9$/L | : | 33 |
| DAYS UNTIL PLATELETS >100 X $10^9$/L | : | 33 |

| | | |
|---|---|---|
| COMPLICATIONS DURING ABMT | : | |
| POSITIVE MICROBIOLOGY ISOLATES | : | Candida; Throat/Coag -ve staph, Staph aureus; Blood, H.S./ Strep faecalis; Blood |
| STATUS POST ABMT | : | CR |
| TREATMENT POST ABMT | : | FURTHER CYTOTOXICS |
| COMPLICATIONS POST ABMT | : | |
| DATE OF RELAPSE | : | 29.9.85 |
| SITE OF RELAPSE | : | CNS |
| DATE OF DEATH | : | |
| CAUSE OF DEATH | : | |
| CURRENT STATUS | : | ALIVE & WELL |

# APPENDIX III

## ~~PUBLISHED PAPERS~~

1. Very high dose chemotherapy with autologous bone marrow rescue in adult patients with resistant lymphoma.
C.C. Anderson, A.H. Goldstone, R.L. Souhami, D.C. Linch, P.G. Harper, K.A. MacLennan, M. Jones, S.J. Machin, A.M. Jelliffe, J.C. Cawley & J.D.M. Richards.
Cancer Chemotherapy and Pharmacology, 1986, 16, 170-175.

2. Double autografting : A potential curative regimen for acute leukaemia?
C.C. Anderson, D.C. Linch & A.H. Goldstone.
Minimal Residual Disease in Acute Leukaemia : 1986.
Martinus Nijhoff Publishers B.V., 1986, 221-233.

3. A rise in the percentage of large unstained cells in the peripheral blood determined by the Hemalog D90 automated differential counter is a feature of impending myeloid engraftment following bone marrow transplantation.
P.J. Martin, C.C. Anderson, H.M. Jones, A. Lai, D.C. Linch & A.H. Goldstone.
Clinical and Laboratory Haematology, 1986, 8, 1-8.

4. Autologous bone marrow transplantation following high dose chemotherapy for the treatment of adult patients with acute myeloid leukaemia.
A.H. Goldstone, C.C. Anderson, D.C. Linch, I.M. Franklin, B.J. Boughton, J.C. Cawley & J.D.M. Richards.
British Journal of Haematology, 1986, 64, 529-537.

5. Autologous bone marrow transplantation ( ABMT ) for both acute myeloid leukaemia ( AML ) and acute lymphoblastic leukaemia ( ALL ) : A comparison.
C.C. Anderson, A.H. Goldstone, D.C. Linch, H.M. Jones, I.M. Franklin, B.J. Boughton, J.C. Cawley & J.D.M. Richards.
Bone Marrow Transplantation, in press.

# DOUBLE AUTOGRAFTING: A POTENTIAL CURATIVE REGIMEN FOR ACUTE LEUKAEMIA?

C.C. Anderson, D.C. Linch & A.H. Goldstone, for the Bloomsbury Transplant Team.

## INTRODUCTION

The conditioning regime used for allogeneic bone marrow transplantation in acute leukaemia has two functions: firstly to serve as immunosuppressive therapy to prevent rejection of the allogeneic marrow and secondly to eradicate host disease. The conditioning regimen most commonly used is TBI given as a single dose or in fractions to a total dose of 9-12 Grays together with cyclophosphamide 60mg/kg on two consecutive days as pioneered by the Seattle transplant unit, (Thomas et al, 1975).

Rejection of a marrow graft following this regimen in patients allografted for acute leukaemia is rare.

Relapse however, still remains a problem. In patients with acute myeloid leukaemia, (AML), treated by allografting in first remission the incidence of relapse is reported to be between 10 and 25%, (O'Reilly RJ, 1983; Deeg et al, 1984). The majority of relapses occurring in the first two years post graft, although relapse has been reported even six years later, (Deeg et al, 1984). Fewer patients with acute lymphoblastic leukaemia,(ALL), have been allografted in first remission but there is the suggestion that relapse is more frequent than in AML. In patients with AML and ALL allografted after first remission the relapse rate is higher, (Appelbaum et al, 1983; Deeg et al, 1984), with five year survival of less than 27% in ALL with leukaemic relapse being the commonest cause of death, (Thomas et al, 1983).

In the first 100 patients transplanted in Seattle for acute leukaemia in relapse, a time at which the leukaemic burden would be high, and the disease is more likely to be resistant than early in first remission, the majority of patients surviving the procedure relapsed.

Twelve patients, not only achieved a CR but remain in remission many years later, (Thomas ED, 1983). This approach is therefore capable of eradicating disease in a small proportion of patients with relapse but there is no way of determining which patients will be cured and which will relapse.

Autologous bone marrow grafting has the advantage that immune mediated graft rejection does not occur.

There are therefore two main problems to consider when deciding on a suitable conditioning regimen for ABMT: the eradication of disease in the patient as in the allograft situation and the eradication of residual disease in the marrow. The absence of a graft-versus-leukaemia, (GVL), effect, (Weiden et al, 1981), in autografting may

mean that an even stronger ablative regimen is required than cyclophosphamide and TBI.

The same pre-graft conditioning as for allografts has been used for autologous bone marrow transplantation, (ABMT), (Burnett et al, 1984). Alternatively a combination chemotherapy regimen has been used. The autologous marrow has been used unpurged, (Gorin et al, 1985; Burnett et al, 1984), or has been purged, 'in vitro', in an attempt to remove the presumed residual disease, (Ritz & Schlossman, 1982; Laporte et al, 1984), although the need for purging has not yet been proven.

There is as yet no convincing evidence of benefit from, 'purging' the autologous marrow in any situation, (Gorin et al, 1985), and for AML in particular there is no evidence of altered sensitivity of leukaemic cells from normal progenitor cells when treated with cytotoxic drugs, 'in vitro', (Douay et al, 1984), nor is there a suitable monoclonal antibody available which can distinguish between these cell types.

We have chosen a double autograft technique as a means of addressing both leukaemic eradication in the host and purging of the marrow.

Eradication of residual leukaemia in the host: If a single dose of massive chemo/radiotherapy may eradicate disease in some but not all patients, then to repeat the procedure should produce a greater tumour kill. TBI cannot be repeated a second time and is therefore an unsuitable modality for a double protocol. We therefore decided on a sequential combination chemotherapy protocol using the same drug regimen for the first and second ABMT.

Eradication of residual leukaemia in the marrow: We argued that a double protocol would effect a form of 'in vitro' purging. For example if the marrow at the time of first harvest contained x tumour cells then post harvest the cryopreserved marrow would contain only 2% x assuming a harvest of 2% of the total marrow content and no differential loss of disease and normal stem cells during cryopreservation. The repopulated marrow would contain only 2% of x if the regrowth of leukaemic and normal cells was the same, so at the second harvest if a further 2% of the marrow were harvested, then the second marrow innoculum would contain only 0.04% of the original leukaemic mass. However, the success of induction regimes which render the patients marrow severely hypoplastic suggests that normal haemopoietic tissue has a regenerative advantage to the leukaemic population. This would make the residual proportion of leukameic cells post double ABMT considerably less than the hypothetical 0.04% postulated above. This might fall below the critical level at which the body's own defences might be able to eliminate or contain any residual disease, total elimination being perhaps unnecessary.

## MATERIALS AND METHODS

### Patients

A total of 42 patients with acute leukaemia have been

treated; 41 adults and one child of six years old. The median age was 35 years. There were 23 males and 18 females. Further details are given in Table I and II.

Twenty-four patients were treated in first remission, 16 with AML and 8 with ALL. The remaining 18 patients were treated during relapse or in a later remission with marrow harvested and stored either in first or subsequent remissions. Eight of these patients had AML and ten had ALL.

Treatment Protocol

The chemotherapy used for both ABMT I and II was the same and is as follows: cyclophosphamide 1.5 G/$m^2$/day, days -5, -4 and -3, adriamycin 50 mg/$m^2$ day -5, BCNU 300 mg/$m^2$ day -5, cytosine arabinoside and thioguanine both 200 mg/$m^2$ given in two divided dosed day -5 to -2 inclusive. The autologous bone marrow was returned on day 0.

Figure 1 shows details of the treatment plan. The first bone marrow harvest was performed, where possible, following recovery from consolidation therapy in first remission patients and as soon as possible following reinduction therapy in the 9 patients harvested and treated in second remission.

Twenty-two of the twenty-four first remission patients were treated within 12 months of their diagnosis with a mean of 8 months, (range 3-23).

Nineteen patients have completed the second part. All had their marrow reharvested as soon as possible after full haematological recovery and proceeded directly to the second treatment, except for one patient who was delayed after harvesting because hospital facilities were temporarily unavailable.

In every case marrow was judged clear of disease by morphological examination of aspirates taken within the five days preceeding the harvest.

The harvested marrow was processed and cryopreserved in liquid nitrogen as previously described, (Linch et al, 1982), and when thawed was reinfused into a central line. The mean number of nucleated cells frozen was 1.89 x $10^8$ cells/kg.

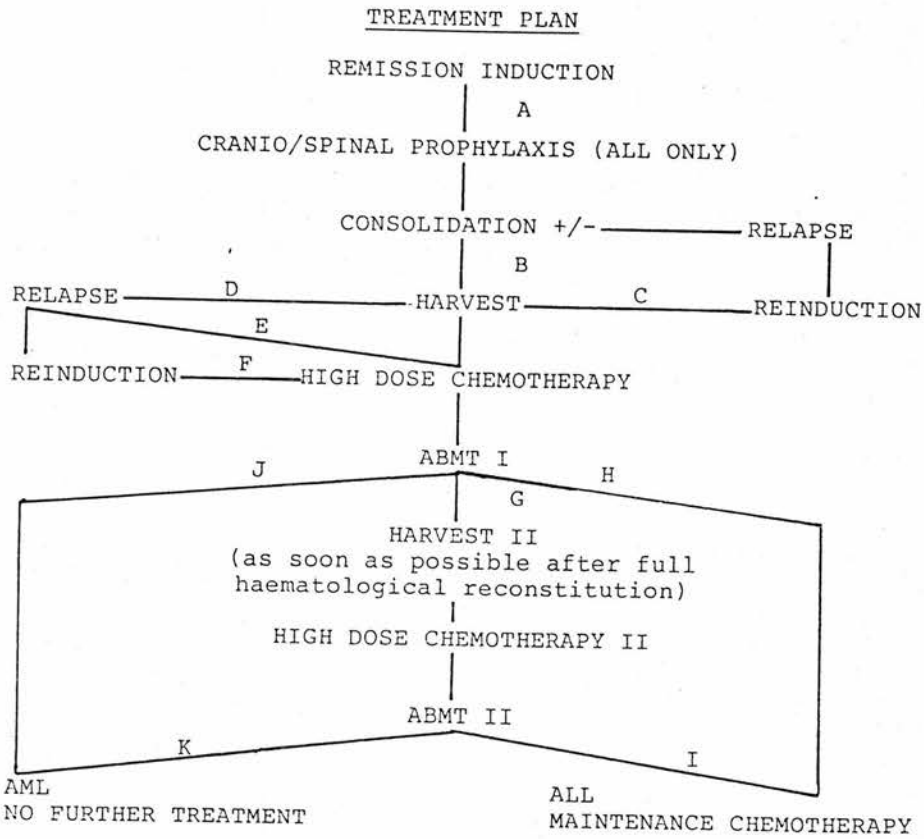
All patients had Hickman central venous catheters inserted prior to starting chemotherapy. All patients receiving very high dose chemotherapy were nursed in single rooms without filtered air precautions. Routine antifungal prophylaxis with oral nystatin or amphotiracin was given.

Some patients also received antibacterial prophylaxis with cotrimoxazole, but this was abandoned in December, 1983 because of increasing bacterial resistance of intestinal flora.

First remission ALL patients had both intrathecal methotrexate and cranial irradiation as CNS prophylaxis prior to ABMT.

Patients with AML received no maintenance therapy post ABMT but patients with ALL were maintained on a regime using methotrexate, mercaptopurine and cytosine arabinoside with three monthly reinduction courses of vincristine

FIGURE 1.




A All patients
B 33 patients harvested in 1st remission
C 8 patients harvested in 2nd remission
D 9 patients harvested in 1st remission but not treated
E 5 patients treated in relapse
F 4 patients reinduced before treatment
G 19 patients who had ABMT II
H 2 patients
I 8 patients
J 15 patients
K 8 patients

and prednisolone for at least two years in view of the evidence that remission is prolonged by continuing maintenance chemotherapy in childhood ALL, (The MRC Trials, 1982), or until relapse, whichever was the sooner.

## RESULTS

### Response to therapy

First remission AML: 16 patients have so far been treated. Eleven, (69%), continue in unmaintained remission day 1705, 1508, 802, 770, 607, 573, 458, 426, 368, 317, with no procedular deaths. Five have relapsed day 35, 68, 191, 229, 322.

First remission ALL: Three of eight patients, (37.5%), remain in remission on maintenance chemotherapy day 816, 562, 292. Three patients, (37.5%), died of infection, one during ABMT I, and two during ABMT II. One patient with T-ALL had a CNS relapse before the second harvest and has since died day 138. The longest survivor, to date, had an extramedullary relapse day 983 and died in relapse in spite of further chemotherapy day 1093.

Others: Four of five patients treated with this regime as reinduction therapy following relapse acheived a complete remission, (CR), the fifth patient died during aplasia of a cerebral haemorrhage. Two patients, (both ALL), went on to receive ABMT II. The other two patients, (both AML), had delayed haematological recovery and did not receive ABMT II. All have relapsed and died except for one patient with ALL who received both ABMT I and II and is still in second remission day 1239.

Eleven patients treated in second remission have died, ten in relapse (day 126, 197, 240, 245, 257, 263, 352, 436, 515), one died of aspergillus pneumonia day 124 during the aplasia induced by ABMT II. The remaining patient with ALL continues in second remission, (day 507).

The one patient treated in third remission relapsed, (day 144), and died.

### Haematological recovery

Details of recovery are given in Table III.

Assays of GM-CFC on the harvested marrow were unhelpful in predicting the speed of engraftment, (Anderson et al, 1985).

### Morbidity

One death from a cerebro-vascular accident day 12 post ABMT I before platelet recovery.

Four deaths were attributed clinically to rapidly progressive pneumonias, although Aspergillus fumigatus was the only organism isolated and this from only one of them.

Non-fatal infections were the commonest complications, with a pyrexia of >38 °C in forty patients, (95%), receiving ABMT I, and in all patients during ABMT II.

Cytotoxic induced nausea and vomiting occurred in all patients but was not usually severe.

Two patients were thought to have cardiotoxicity: one patient, (UPN 164), who developed pericarditis post chemotherapy, and one other, (UPN B4), who developed left ventricular failure necessitating omission of the final dose of cyclophosphamide.

One patient suffered a grand mal convulsion which was never fully explained. Greater details of these complications are to be published elsewhere, (Anderson et al, 1985).

## DISCUSSION

Eleven, (69%), of our patients with AML who were treated with the ABMT protocol in first remission as intensive consolidation therapy remain in unmaintained remission with a median follow up of eighteen months, (range 11-56 months), post ABMT. These results are as good as or better than most reported results of conventional chemotherapy protocols in adult patients, (Weinstein et al, 1983).

The five relapses have occurred in patients who had only ABMT I, none as yet occurring in the group who had both ABMT I and II. Numbers are small and a longer follow up period is required to draw any conclusions.

Maraninchi et al, 1984, have also advocated a double protocol. Four of their five long term survivors had ABMT I and II, (11+, 11+, 28+, 29+), and of ten relapses eight patients received only ABMT I.

The collective EBMT date, (Gorin et al, 1985), which includes patients from both our own group and those reported by Maraninchi et al, 1984, showed a trend in favour of double autografting when compared to single autografts when comparing disease free survival: 79% versus 48% at 640 days, ($p<0.1$). Numbers are small and the differences do not acheive statistical significance. If encouraging results are maintaned it will not be possible to determine if this is due to improved leukaemia eradication or 'in vivo' purging. This will depend on the development of sensitive assays for minimal residual disease.

Studies from our own institution, (Souhami et al, 1985), have attempted to assess the increase in tumour kill in a solid tumour - small cell carcinoma of the lung when treated with a double ABMT protocol. Tumour volumes were measured by thoracic computed tomographic, (CT), scan before and after each cycle of high dose cyclophosphamide. The average decrease in tumour volume was from 99.2 cc to 21 cc post ABMT I and reduced further to only 14.1 cc post ABMT II. When compared to an earlier study using ABMT I only, the double procedure did not increase the response rate or prolong the survival. The results were assumed to imply rapid emergence of drug resistance after a single cycle of high dose chemotherapy. In acute leukaemia we hope the malignant cells may be different, or that a combination chemotherapy protocol will result in a smaller chance of producing a drug resistant clone.

The small number of patients with ALL treated in first CR are inadequate to draw any conclusions in this disease.

Sixteen of our patients treated beyond first CR have relapsed within 13 months of ABMT. Only eight of these patients received ABMT I and II. Only two remain in CR, one who was treated with ABMT I only, (day 507), and one who received both ABMT I and II, (day 1239). It seems likely this represents failure to eradicate host disease as has been found following allografting, (Thomas et al, 1983).

The relapse of five, (50%), of patients with AML treated in first CR who did not have ABMT II whilst there are no relapses in the six patients who had ABMT I and II could mean that the second ABMT has resulted in a greater reduction of host disease. It could also mean that delay in haematological recovery after ABMT I which was the main reason for failing to preceed to ABMT II may be a characteristic of more aggressive or resistant disease and such patients may be a poor prognosis group, irrespective of whether they receive ABMT II or not.

We are encouraged by our data in first remission AML to hope there may be an 'in vivo' purging effect and to employ ABMT II whenever possible.

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TABLE I

01.09.85

PATIENT CHARACTERISTICS

1ST REMISSION AML

| UPN | SEX | AGE | FAB CLASS | NO. OF GRAFTS | DIAG. ->CR | CR-> ABMT | DIAG-> ABMT | RESULT ABMT->REL | SURVIVAL POST ABMT | TOTAL SURV. | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | M | 25 | M1 | 2 | 2 | 2 | 4 | CR | 56+ | 60+ | A & W |
| 30 | M | 38 | M3 | 1 | 1 | 7 | 8 | CR | 50+ | 58+ | A & W |
| 103 | F | 43 | M4 | 2 | 2 | 5 | 7 | CR | 26+ | 34+ | A & W |
| 108 | F | 39 | M1 | 2 | 2 | 7 | 9 | CR | 25+ | 34+ | A & W |
| 128 | F | 32 | M2 | 1 | 1 | 5 | 6 | CR | 20+ | 25+ | A & W |
| 131 | F | 45 | M4 | 1 | 3 | 5 | 8 | CR | 19+ | 27+ | A & W |
| 132 | M | 47 | M1 | 1 | 2 | 4 | 6 | CR 11 | 18+ | 24+ | Relapse |
| B3 | M | 42 | M4 | 1 | 3 | 1 | 4 | CR 2 | 3 | 7 | DEAD |
| B4 | F | 55 | M2 | 1 | 3 | 10 | 13 | CR 6 | 8 | 21 | DEAD |
| 143 | M | 49 | M1 | 2 | 1 | 3 | 4 | CR | 15+ | 19+ | A & W |
| 147 | M | 35 | M5 | 2 | 2 | 4 | 6 | CR | 14+ | 20+ | A & W |
| 148 | M | 26 | M1 | 2 | 1 | 6 | 7 | CR | 14+ | 20+ | A & W |
| 156 | F | 19 | M2 | 1 | 3 | 9 | 12 | CR | 12+ | 25+ | A & W |
| 161 | M | 36 | M1 | 1 | 2 | 7 | 9 | CR | 11+ | 20+ | A & W |
| 163 | F | 36 | M4 | 1 | 4 | 2 | 6 | CR 8 | 10+ | 16+ | Relapse |
| 174 | F | 40 | M2 | 1 | 3 | 4 | 7 | REL | 6 | 13 | DEAD |

TABLE I (Continued)

1ST RELAPSE OR 2ND REMISSION

| UPN | SEX | AGE | FAB CLASS | NO. OF GRAFTS | DIAG. ->CR | CR-> ABMT | DIAG-> ABMT | RESULT ABMT->REL | SURVIVAL POST ABMT | TOTAL SURV. | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 41*° | F | 57 | M2 | 1 | 2 | 20 | 22 | CR 7 | 10 | 32 | DEAD |
| 55 | F | 31 | M1 | 1 | 2 | 5 | 7 | CR 2 | 8 | 15 | DEAD |
| 92*° | M | 49 | M1 | 1 | 3 | 22 | 25 | NE Died day 12 | | 25 | DEAD |
| 98 | M | 44 | M1 | 2 | 6 | 4 | 10 | CR 8 | 9 | 19 | DEAD |
| 100*° | M | 51 | M5 | 1 | 2 | 6 | 8 | CR 3 | 3 | 11 | DEAD |
| 122 | F | 34 | M5 | 1 | 1 | 6 | 7 | CR 2 | 7 | 14 | DEAD |
| 125* | M | 21 | M1 | 2 | 2 | 35 | 37 | CR 5 | 6 | 43 | DEAD |
| 129 | M | 51 | M6 | 1 | 1 | 35 | 36 | CR 13 | 14 | 50 | DEAD |

* Patients who were harvested in 1st remission.

° Patients who were treated in 1st relapse.

TABLE II

01.09.85

PATIENT CHARACTERISTICS

1ST REMISSION ALL

| UPN | SEX | AGE | FAB/IM CLASS | NO. OF GRAFTS | DIAG. ->CR | CR-> ABMT | DIAG-> ABMT | RESULT ABMT->REL | SURVIVAL POST ABMT | TOTAL SURV. | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 57 | M | 23 | T-ALL | 1 | 1 | 3 | 4 | REL-2 | 4 | 8 | DEAD |
| 69 | F | 24 | ALL | 2 | 1 | 4 | 5 | CR 33 | 37 | 42 | DEAD |
| 103 | M | 16 | cALL | 2 | 2 | 6 | 8 | CR | 27+ | 35+ | A & W |
| B1 | M | 18 | cALL L1 | 2 | 1 | 10 | 11 | NE Died day 146 | 5 | 16 | DEAD |
| B2 | F | 49 | cALL L1 | 2 | 2 | 15 | 17 | CR | 18+ | 36+ | A & W |
| 150 | M | 46 | cALL | 2 | 2 | 1 | 3 | NE Died day 88 | 3 | 6 | DEAD |
| 157 | M | 22 | cALL L2 | 1 | 7 | 2 | 9 | NE Died Day 23 | 1 | 10 | DEAD |
| 164 | M | 16 | ALL L2 | 1 | 1 | 3 | 4 | CR | 10+ | 13+ | A & W |

1ST RELAPSE, 2ND OR 3RD REMISSION

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 39*° | M | 19 | ALL | 2 | 1 | 32 | 33 | CR 5 | 8 | 41 | DEAD |
| 51*° | F | 35 | cALL | 2 | 1 | 58 | 59 | CR | 42+ | 101+ | A & W |
| 67* | F | 23 | ALL | 1 | 2 | 17 | 19 | CR 7 | 6 | 25 | DEAD |
| 90 | M | 6 | T-ALL | 2 | 1 | 5 | 6 | CR 3 | 8 | 14 | DEAD |
| 96* | M | 23 | cALL | 1 | 1 | 27 | 28 | CR 2 | 4 | 32 | DEAD |
| 107* | M | 47 | cALL | 2 | 2 | 39 | 41 | CR 10 | 11 | 52 | DEAD |
| 118 | F | 22 | NULL ALL | 2 | 2 | 41 | 43 | CR 9 | 17 | 60 | DEAD |

TABLE II (Continued)

| UPN | SEX | AGE | FAB/IM CLASS | NO. OF GRAFTS | DIAG. ->CR | CR-> ABMT | DIAG-> ABMT | RESULT ABMT->REL | SURVIVAL POST ABMT | TOTAL SURV. | CURRENT STATUS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 121 | M | 38 | T-ALL | 2 | 2 | 30 | 32 | NE Died day 124 | 4 | 36 | DEAD |
| 135 | F | 13 | ALL | 1 | | | 31 | CR | 19+ | 49+ | A & W |
| B5** | F | 19 | ALL L2 | 1 | 1 | 59 | 60 | CR 5 | 8 | 68 | DEAD |

* Patients who were harvested in 1st remission

° Pateitns who were treated in 1st relapse

** Patient who was harvested and treated in 3rd remission

TABLE III

HAEMATOLOGICAL RECOVERY IN DAYS. (Day 0=ABMT).

ABMT I ONLY - ALL PATIENTS (n=42)

| | | RANGE |
|---|---|---|
| Total WBC >1000 x 10/l | 19 | 12 - 40 |
| Neutrophils >500 x 10/l | 23 | 14 - 52 |
| Platelets >50 x 10/l | 36 | 13 -228 |
| Nucleated cells x 10/kg | 1.9 | 0.6 - 3.1 |

1 patient died before recovery - his results are therefore not included.

1 patient died before platelet recovery - his WBC results only are included.

COMPARISON OF ABMT I VS II (n=19)

| | ABMT I | RANGE | ABMT II | RANGE |
|---|---|---|---|---|
| Total WBC >1000 x 10/l | 17 | 11 -28 | 23 | 13 -41 |
| Neutrophils >500 x 10/l | 21 | 12 -39 | 27 | 14 -45 |
| Platelets >50 x 10/l | 24 | 13 -39 | 38 | 20 -58 |
| Nucleated cells x 10/kg | 1.8 | 0.6- 3.2 | 1.9 | 1.0- 4.0 |
| GM-CFC x 10/kg | 5.8 | 0.7-13.6 | 5.3 | 0.9-15.0 |

3 patients died before recovery in ABMT II - their results are not included.

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# A rise in the percentage of large unstained cells in the peripheral blood determined by the Hemalog D90 automated differential counter is a feature of impending myeloid engraftment following bone marrow transplantation

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*Summary* The early phase of bone marrow regeneration has been monitored by automated differential counts on the peripheral blood using a Hemalog D90, following 107 transplant procedures. An elevated percentage of large unstained cells (LUCs) was detected in over 98% of cases and in 72% of cases the rise in percentage LUCs preceded the rise of the total leucocyte count into the detectable range on a Coulter counter ($> 0.3 \times 10^9$/l) by an average of 4 days. These LUCs are shown to be CD8+T lymphocytes. The ability to detect the earliest signs of regeneration is particularly useful when regeneration is delayed and repeat marrow infusion is considered.

Keywords: automated differential counts, large unstained cells, bone marrow transplantation

Previous investigations of marrow regeneration following bone marrow transplantation have focused on the time of neutrophil and platelet recovery to a fixed value, (Goldstone *et al.* 1983) or on the lymphocyte subpopulation imbalances that arise (De Bruin *et al.* 1981, Bacigalupo *et al.* 1981, Linch *et al.* 1983, Ansley & Orstein 1970). In this report the very earliest phases of regeneration detected in the peripheral blood have been studied. Automated cell counters such as the Coulter S and the Hemalog D90 only give a reliable white cell count above $0.3 \times 10^9$/1 but the Hemalog D90 will produce a very accurate and reproducible differential count at white cell counts below this value (Ansley & Ornstein 1970). The automated Hemalog D90 differential count was therefore

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determined serially in a large number of autologous and allogeneic bone marrow recipients and the patterns obtained related to the leucocyte recovery into the measureable range.

## Materials and methods

### *Preparation of mononuclear cells*

Mononuclear cells were prepared from heparinized peripheral blood by density separation on ficoll hypaque (SG = 1.077).

### *Cell morphology*

This was assessed on standard blood films and cytospin preparations of mononuclear cells using May Grunwald Giemsa stain.

### *Immunological phenotyping*

Mononuclear cell aliquots were stained with mouse monoclonal antibodies and fluorescent conjugated goat antimouse immunoglobulin (Nordisc Ltd.) as previously described (Linch *et al.* 1982). Stained cells were analysed on a fluorescent activated cell sorter (FACS IV). The leucocyte phenotype was also assessed on air dried films or cytospin preparations using the alkaline phosphatase—anti-alkaline phosphatase technique (Cordell *et al.* 1984). Adequate controls were always used to exclude endogenous alkaline phosphatase activity and non-specific binding of antibody. Alkaline phosphatase cytochemistry was finally performed with naphthol AS-B1 phosphoric acid as substrate (pH 9.2), fast red TR as the capture agent and haematoxylin as the counter stain.

### *Monoclonal antibodies*

UCHT1 was used as an anti-CD3 reagent and was kindly provided by PCL Beverley. Anti-CD4 (Leu 3a) and anti-CD8 (Leu 2a) antibodies were obtained from Becton Dickinson. UCHM1 stains 80% of normal monocytes and 'promonocytes' as determined by analysis of monocytic leukaemias (Linch *et al.* 1984), and was provided by PCL Beverley. Leu M3 (Becton Dickinson) was used as a further monocyte specific reagent. $DA_2$ was used to detect non-polymorphic determinants of HLADR (Brodsky *et al.* 1979). Monoclonal anti alkaline phosphatase was provided by PCL Beverley.

### *Patients*

Eighty patients received 107 transplant procedures with survival to a stage at which evidence of haemopoietic regeneration was detectable. Of these patients 76

were adults and 48 were male. Eleven patients received allogeneic marrow from an HLA-matched sibling for acute leukaemia (9 cases) aplastic anaemia (1 case) and congenital mucopolysacharridosis (1 case). Patients with acute leukaemia were conditioned with cyclophosphamide and single fraction total body irradiation (1000 cGys) and the patients with aplastic anaemia and mucopolysacharridosis with cyclophosphamide and cyclophosphamide plus busulphan respectively. Sixty-nine patients received high dose chemotherapy and cryopreserved autologous bone marrow rescue as treatment for acute leukaemia (25 patients) small cell carcinoma of the lung (32 patients) carcinoma of the ovary (8 cases) and lymphoma (4 cases). Twenty-seven patients received two high dose chemotherapy and autologous bone marrow transplant procedures. The details of the different protocols have been published elsewhere (Souhami *et al.* 1983, Goldstone *et al.* 1984a, b).

*Assessment of haemopoietic recovery*

Blood samples from all patients were evaluated for haematological recovery by daily cell counts on a Coulter Counter S Plus. Automated cytochemistry was also performed on a Hemalog D90. Patients included early in the study had fewer Hemalog D counts, but efforts were made to obtain daily counts in the later patients during the early regenerative period. The principles of the Hemalog D90 automated cytochemistry system have been previously described (Ansley & Orstein 1970, Mansberg *et al.* 1974). White cells are differentiated by their light scattering and light absorption characteristics against preset electronic thresholds on three separate channels (peroxidase, non-specific esterase and Astra Blue). The non-specific esterase and the Astra Blue stain count monocytes and basophils respectively. The peroxidase channel is more complex, not only counting peroxidase positive cells, neutrophils, eosinophils, monocytes and basophils, but also the non-staining cells of the lymphocyte and primitive myeloid lineage. The light scatter patterns recognize cell size and the specific staining reaction of cells is interpreted by light absorption.

One component of this automated differential white cell count is an electronic threshold area into which large cells having no cytochemical staining are counted (LUCs). This group of large unstained cells is usually considered to be part of the lymphocyte population if it falls within the normal range (0.8–3.1%). However, when this cell component is elevated immature cell types and atypical lymphoid cells must be considered and a May-Grunwald Giemsa stained blood film examined.

The high level of precision of the differential white cell count in leucopenic patients using this technique has previously been reported (Ross & Bardwell 1982). In leucopenic patients with an absolute neutrophil count of $0.5 \times 10^9/1$ the coefficient of variation is 8% compared to a 20% coefficient of variation using manual methods of differential white cell count.

## Results

### *Detection of LUCs following transplantation*

An elevated percentage LUC count was detected following 105 transplant procedures. In only two cases was a rise in the percentage of LUCs not detected. Serial counts were available in 78 cases and in these cases the mean peak LUC count was 19.3% ± (SE) with a range of 3.2–56.8%.

The relationship of the rise in total white cell count to the rise in percentage of LUCs is shown for all 105 cases in which a rise occurred (Figure 1). In 72% of the 78 cases in which serial data was available, the rise in LUCs preceded the rise in WBC by an average of 4 days. In 23 further cases in which the serial data is incomplete but evaluable in this respect, 20 also showed a rise in the percentage of LUCs predating the rise in WBC. In 17% the rise in LUCs and WBC were simultaneous and only in 8% of cases did the rise in WBC predate the rise in LUC percentage. The relationship between the rise in percentage of LUCs and rise in total WBC was similar for both allografts and autografts (Table 1). The autologous transplants were performed in cases of acute leukaemia, resistant lymphoma and solid tumours (small cell cancer of the lung and ovarian carcinoma). Regeneration was more delayed in the cases autografted for acute leukaemia; the time to reach a leukocyte count $> 0.5 \times 10^9/1$ was 24.3 days compared to 11.4 days in the remainder. Patients with solid tumours were autografted as first line treatment and received the lowest levels of ablative chemotherapy; regeneration was invariably rapid in this group. Nonetheless, despite these differences the rise in percentage of LUCs still predated the rise in WBC by a similar time, being 4.0, days in acute leukaemia, 3.0, days in patients with lymphoma and 4.1 days in patients with solid tumours. This time interval in the allografts was an average of 3.9 days.

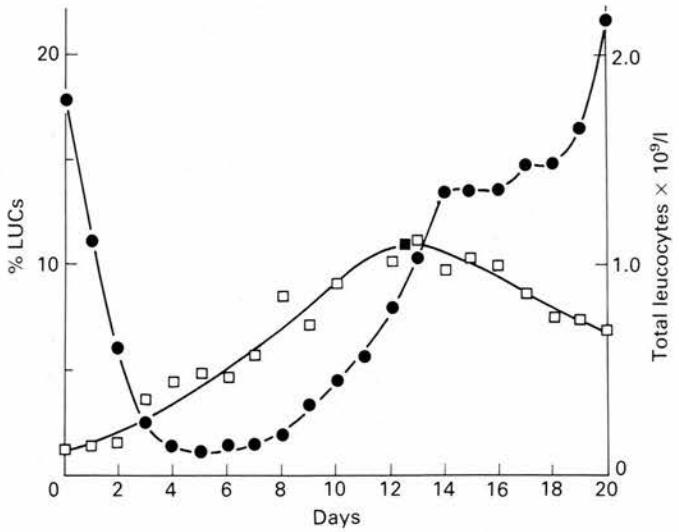


**Figure 1.** Appearance of total leukocytes and LUCs in the blood following allogeneic and autologous bone marrow transplantation. ●, Total leucocytes; □, % LUCs. Values shown are means ± SE following 94 transplant procedures.

**Table 1.** Relationship of rise in WBC to rise in LUC

| | | Followed LUC rise | Simultaneous with LUC rise | Preceded LUC rise | No LUC rise |
|---|---|---|---|---|---|
| Transplant procedure | | | | | |
| Allogeneic | 11 | 8 | 0 | 2 | 1 |
| Autologous | 67 | 48 | 13 | 5 | 1 |
| Totals | 78 | 56 | 13 | 7 | 2 |

Two patients showed regeneration of leucocytes without a rise in percentage of LUCs. Both of these patients had ALL and suffered from opportunistic lung infections. The significance of this is not clear.

In only two cases in which a rise in LUC was noted was there failure of the WBC to rise. In one case this was due to death from an intracerebral haemorrhage on day 12 at a time when the percentage of LUCs was rising but the WBC had not risen above $0.3 \times 10^9/1$. In the other case the percentage of LUCs rose to a peak of 22% on day 19 and then fell back to the normal range by 28 days. This patient developed an Aspergillus pneumonia during the regeneration period and died on day 33 without a leucocyte count ever rising above $0.3 \times 10^9/1$.

Six patients received repeated granulocyte infusions for uncontrolled sepsis early after transplantation before evidence of regeneration. In no instance was there a rise in the percentage of LUCs detected.

*The nature of LUCs*

Careful inspection of blood films with very high percentage LUC counts, during the early regeneration period, reveals that these cells are large mononuclear cells, often with indented nuclei showing some chromatin condensation but no nucleoli. They have moderate quantities of faintly basophilic cytoplasm which contain no obvious granules. These cells most commonly resemble monocytes, but LUCs are by definition non-specific esterase (NSE) and peroxidase negative. This NSE negativity has been confirmed by manual techniques. Furthermore, adherence for 1 h to plastic of ficoll hypaque separated mononuclear cells did not reduce the percentage of LUCs as determined by re-analysis on the Haemalog D90 in two cases tested.

In four further cases, adherent cell depleted mononuclear cells containing more than 10% LUC were phenotyped with a range of monoclonal antibodies. The predominant cell type present was a CD8+T cell (Mean CD3%, 47%; mean CD8%, 42%). B cells as detected by anti-B1 represented only 3.5% of cells. There were no monocytic cells detected by staining with UCHM1 or Leu M3.

In one case over 20% of all leucocytes before separation were LUCs. Mononuclear cells from this patient were analysed on a FACS IV and 34% of

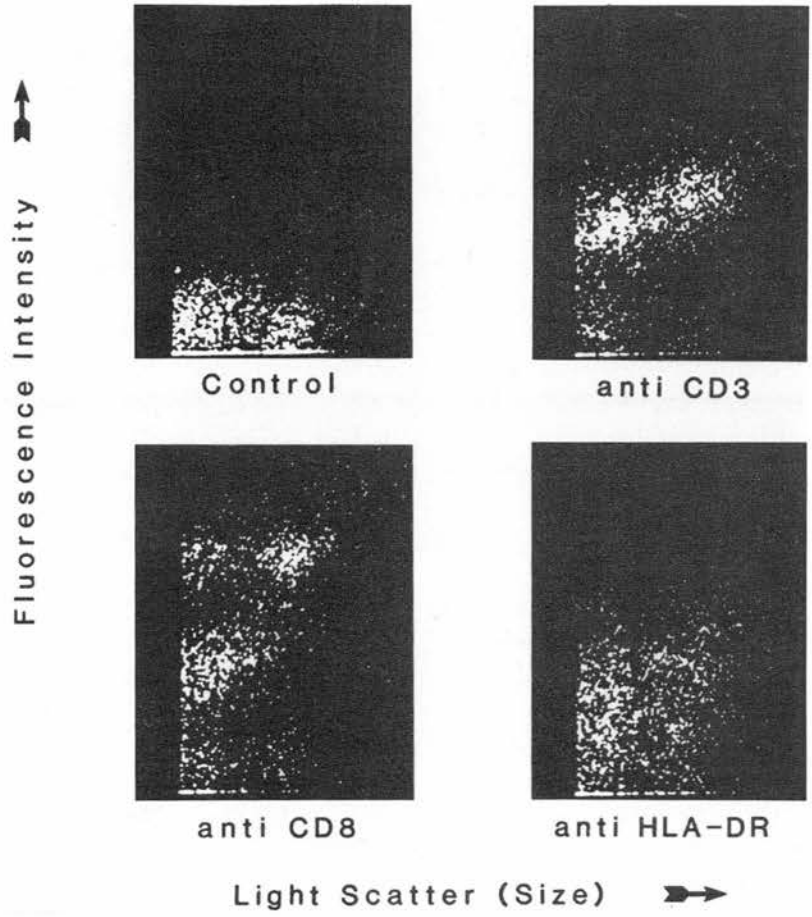


**Figure 2.** Size and fluorescence profiles of peripheral blood mononuclear cells in the early stages of engraftment.

cells were found to be large cells distinct in size from a typical lymphocyte (Figure 2, control). Analysis of the fluorescence profiles revealed that virtually all the large cells were CD3+ CD8+T cells (Figure 2, anti CD3 and anti CD8). Approximately half the large cells expressed HLA-DR antigens (Figure 2, anti HLA-DR). This CD3+ CD8+ phenotype of the large mononuclear cells in the early regenerative period was confirmed in five further cases by immunohistological staining of blood smears.

## Discussion

A rise in the percentage of LUCs counted on the Haemalog D is indicative of successful engraftment following bone marrow transplantation. In 72% of cases this rise can be detected before the rise in total leucocyte count ($> 0.3 \times 10^9/l$) can be reliably measured on the Coulter counter. In these cases the rise in

percentage of LUCs is detected an average of 4 days before the leucocyte rise. In only one case surviving long enough for evaluation was a rise in the percentage of LUCs not followed by subsequent engraftment. This patient had developed a fungal pneumonia and it is likely that this caused toxic suppression of the graft after early engraftment had already commenced. Serial marrow biopsies were not performed and firm support for this hypothesis that the percentage rise in LUC predicted impeding myeloid engraftment is lacking. This information is frequently of value to the clinician, particularly when engraftment is slow, the patient is sick and re-infusion of further marrow is being considered. This applies to allografts and autografts in which only half the harvested marrow was reinfused (lymphoma protocol in this study). It is in this context worthy of note that granulocyte transfusions did not cause a rise in the percentage of LUCs which might falsely have been interpreted as evidence of engraftment. The kinetics of early engraftment were similar in autografts and allografts regardless of the underlying disease, although the time to reach $0.5 \times 10^9/1$ neutrophils in the peripheral blood was delayed in the patients with acute leukaemia receiving autografts.

Regeneration was generally rapid in the patients treated for small cell carcinoma of the lung and it appears that the marrow reinfusion did not lessen the period of aplasia. It is probable that regeneration came from stem cells surviving chemotherapy rather than from the infused autologous marrow and that the initial rise in the percentage of LUCs is a feature of recovery from severe myelosuppression rather than a feature of transplantation *per se*. In support of this view, we have also noted an initial rise in the percentage of LUCs in the regenerative phase of patients receiving heavy leukaemia induction therapy without marrow support.

The LUCs, although of monocytoid appearance, are shown to be T lymphocytes of the CD8+ subset. We have previously shown that CD8+ lymphocytes predominate in the peripheral blood after both autologous and allogeneic marrow transplants (Linch *et al.* 1983) and it is now apparent that in the majority of cases this type of lymphocyte is among the first to appear in the blood. It is possible that this initial T cell expansion may facilitate myeloid engraftment. There is some evidence that extensive T cell depletion of donor marrow for the prevention of graft versus host disease may lead to delayed engraftment and even graft failure in some cases (Waldmann *et al.* 1984). It will be of considerable interest to study the kinetics of early engraftment using the Hemalog D after such T cell depletion procedures.

*Note added in proof.* The possibility that these CD8+ cells are NU cells remains to be explored.

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# Autologous bone marrow transplantation following high dose chemotherapy for the treatment of adult patients with acute myeloid leukaemia

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SUMMARY. 24 adult patients with acute myeloid leukaemia (AML) were treated with intensive chemotherapy followed by autologous marrow rescue. The procedure was repeated twice in eight patients. 11 of 16 patients treated in first remission continue in first unmaintained remission (9–54 months, median 17 months). Eight patients treated at relapse or second remission have relapsed again and died within 14 months of their first autologous bone marrow transplant (ABMT). This form of intensification therapy would appear valuable for adult AML patients in first remission.

The prognosis for adult patients with acute myeloid leukaemia in first remission remains poor on conventional chemotherapy protocols (Lister & Rohatiner, 1982) and once relapse has occurred few patients have extended survival. Allografting is a feasible proposition for only a small proportion of patients (i.e. those of young age with HLA-matched donor). Autologous bone marrow transplantation (ABMT) is in contrast available to all patients in remission less than 55 years of age. The mortality from such an approach may be no greater than recent intensive consolidation/late intensification regimes and morbidity may be less due to the shorter treatment period (Weinstein *et al*, 1983). A potential complication of ABMT in leukaemia is of minimal residual leukaemia remaining in the harvested autologous marrow. In this study we have attempted to reduce residual leukaemia and prolong remission by a double grafting procedure using two sequential courses of high dose chemotherapy with autologous marrow rescue.

## PATIENTS AND METHODS

*Patient characteristics.* A total of 24 adult patients with AML have been treated; median age 40 years; 13 males, 11 females. 16 patients had AML treated in first remission, eight

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patients were treated during relapse or second remission with marrow harvested and stored in either first or second remission. Further details are given in Table I.

*Treatment protocol* (see Fig 1). Patients were referred from several centres and although initial therapy was not standardized induction had been achieved with regimes containing a

**Table I.** Patient characteristics

| UPN | Sex | Age (yr) | FAB class. | No. of grafts | Diag. >CR (mth) | Cr> ABMT (mth) | Diag.> ABMT (mth) | Status post ABMT | DFS post ABMT | Total surv. | Current status |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Patients treated with ABMT during first remission | | | | | | | | | | | |
| 19 | M | 25 | M1 | 2 | 2 | 2 | 4 | CR | 54+ | 58+ | A & W |
| 30 | M | 38 | M3 | 1 | 1 | 7 | 8 | CR | 48+ | 56+ | A & W |
| 103 | F | 43 | M4 | 2 | 2 | 5 | 7 | CR | 24+ | 31+ | A & W |
| 108 | F | 39 | M1 | 2 | 2 | 7 | 9 | CR | 24+ | 33+ | A & W |
| 128 | F | 32 | M2 | 1 | 1 | 5 | 6 | CR | 18+ | 24+ | A & W |
| 131 | F | 45 | M4 | 1 | 3 | 5 | 8 | CR | 17+ | 25+ | A & W |
| 132 | M | 47 | M1 | 1 | 2 | 4 | 6 | CR | 11 | 23+ | Relapse |
| B3 | M | 42 | M4 | 1 | 3 | 1 | 4 | CR | 2 | 7 | Dead |
| B4 | F | 55 | M2 | 1 | 3 | 10 | 13 | CR | 6 | 21 | Dead |
| 143 | M | 49 | M1 | 2 | 1 | 3 | 4 | CR | 13+ | 17+ | A & W |
| 147 | M | 35 | M5 | 2 | 2 | 4 | 6 | CR | 12+ | 18+ | A & W |
| 148 | M | 26 | M1 | 2 | 1 | 6 | 7 | CR | 12+ | 19+ | A & W |
| 156 | F | 19 | M2 | 1 | 3 | 9 | 12 | CR | 11+ | 23+ | A & W |
| 161 | M | 36 | M1 | 1 | 2 | 7 | 9 | CR | 9+ | 18+ | A & W |
| 163 | F | 36 | M4 | 1 | 4 | 2 | 6 | CR | 7 | 14+ | Relapse |
| 174 | F | 40 | M2 | 1 | 3 | 4 | 7 | Rel.** | 0 | 13+ | Relapse |
| Patients treated with ABMT as reinduction therapy or in second remission | | | | | | | | | | | |
| 41*/† | F | 57 | M2 | 1 | 2 | 20 | 22 | CR | 7 | 32 | Dead |
| 55 | F | 31 | M1 | 1 | 2 | 5 | 7 | CR | 2 | 15 | Dead |
| 92*/† | M | 49 | M1 | 1 | 3 | 22 | 25 | NE, died Day 12 | | 25 | Dead |
| 98 | M | 44 | M1 | 2 | 6 | 4 | 10 | CR | 8 | 19 | Dead |
| 100*/† | M | 51 | M5 | 1 | 2 | 6 | 8 | CR | 3 | 11 | Dead |
| 122 | F | 34 | M5 | 1 | 1 | 6 | 7 | CR | 2 | 14 | Dead |
| 125* | M | 21 | M1 | 2 | 2 | 35 | 37 | CR | 5 | 43 | Dead |
| 129 | M | 51 | M6 | 1 | 1 | 35 | 36 | CR | 13 | 50 | Dead |

UPN: Unique Patient Number. All patients grafted in the Bloomsbury Transplant Unit have been given consecutive numbers dependent only on the date of ABMT. Where the UPN has been prefixed with a 'B' the patients were grafted at the Queen Elizabeth Hospital, Birmingham. FAB class.: French, American, British classification. CR: Complete remission. DFS: Disease free survival. + indicates continuing survival.

* Patients who were harvested in first remission.

† Patients who were treated in first relapse.

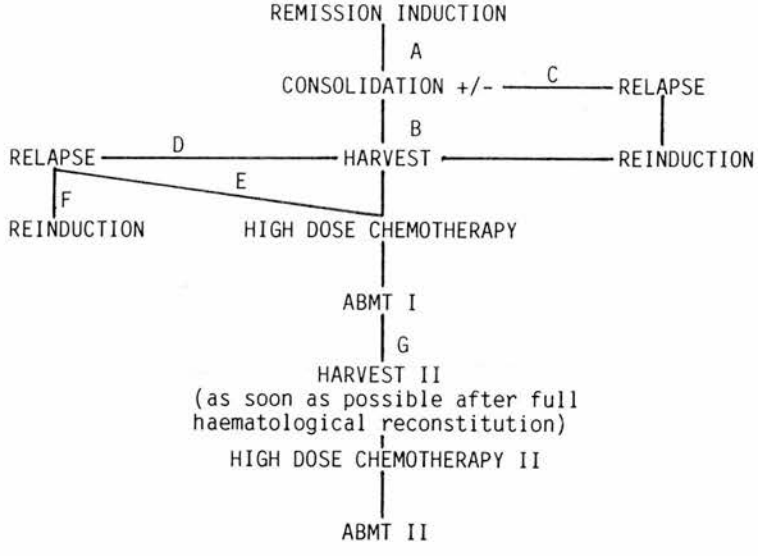
** Although performed in apparent remission this patient regenerated with disease.

central core of daunorubicin, cytosine arabinoside and thioguanine and when these agents had failed other therapy including M-AMSA, VP16 and adriamycin had been introduced. The first bone marrow harvest was performed as soon as possible after consolidation therapy in first remission patients (range 1–9 months) and as soon as possible following reinduction therapy in the four patients harvested and treated in second remission (range 2 d to 4 months). The four patients who were harvested at some stage during first remission and then treated during relapse or second remission had their marrow stored for a median of 223 d (range 201–730 d). The 16 first remission patients had their marrow stored for a mean of 23 d (median 10 d, range 5–107 d) the five second remission patients for a mean of 15 d (range 7–24 d).

All first remission patients were treated with AMBT I within 13 months of their diagnosis (mean 7 months, range 4–13 months) and within 9 months of achieving CR (mean 4 months, range 1–9 months).

In every case, marrow was judged clear of disease by morphological examination of aspirates taken within 5 d of the harvest.

The marrow was harvested, processed and cryopreserved in liquid nitrogen as previously described (Linch *et al*, 1982). The marrow was thawed rapidly and reinfused into a Hickman central venous catheter which had usually been inserted at the time of the original harvest.




A All patients
B 20 patients harvested in 1st remission
C 4 patients harvested in 2nd remission
D 4 patients harvested in 1st remission but not treated
E 3 patients treated in relapse
F 1 patient reinduced before treatment
G 8 patients who had part II

**Fig 1.** Treatment plan.

*High dose chemotherapy regime.* The ablative chemotherapy used for both ABMT I and II was the same and is as follows: cyclophosphamide 1·5 g/m$^2$/d, days −5, −4, −3, adriamycin 50 mg/m$^2$ day −5, BCNU 300 mg/m$^2$ day −5, cytosine arabinoside and thioguanine both 200 mg/m$^2$/d given in two equal doses day −5 to −2 inclusive. The autologous bone marrow was returned on day 0. ABMT II was attempted as soon as full regeneration had occurred from ABMT I but was performed in only six first remission patients and two others grafted at a later stage. The reasons for not performing ABMT II are shown in Table II.

All patients receiving very high dose chemotherapy were nursed in ordinary single rooms without filtered air precautions. Routine antifungal prophylaxis with oral nystatin or amphotericin was given. All had Hickman central catheters inserted prior to starting chemotherapy.

Some patients also received antibacterial prophylaxis with cotrimoxazole, but this was abandoned in December 1983 because of increasing resistance of bacteria on *in vitro* tests of stool cultures and inadequate proof of benefit (Henry *et al*, 1984).

## RESULTS

### *Response to therapy*

*First remission AML.* 16 patients have so far been treated. 11/16 continue in unmaintained remission 54, 48, 24, 24, 18, 17, 13, 12, 12, 11 and 9 months post ABMT, with no procedural deaths. 5/16 have relapsed at 1, 2, 6, 7 and 11 months post ABMT (see Fig 2).

*Others.* Two of three patients treated with this regime as reinduction therapy following relapse achieved a complete remission (CR), neither went on to receive part II because of delayed haematological recovery. Both have relapsed and died (at 4 and 10 months). One patient died during aplasia of a cerebral haemorrhage on day 12.

**Table II.** Reasons for not proceeding to ABMT II

| | |
|---|---|
| Procedural death in part I | 1 |
| Relapse | 4 (1 CNS) |
| Delayed haematological recovery | 5 |
| Refused | 4 |
| Other* | 2 |
| Total | 16 |

* One patient was not reconsidered because of very slow physical recovery after part I. One patient has been delayed because of the finding of a reduced left ventricular ejection fraction on MUGA scan.

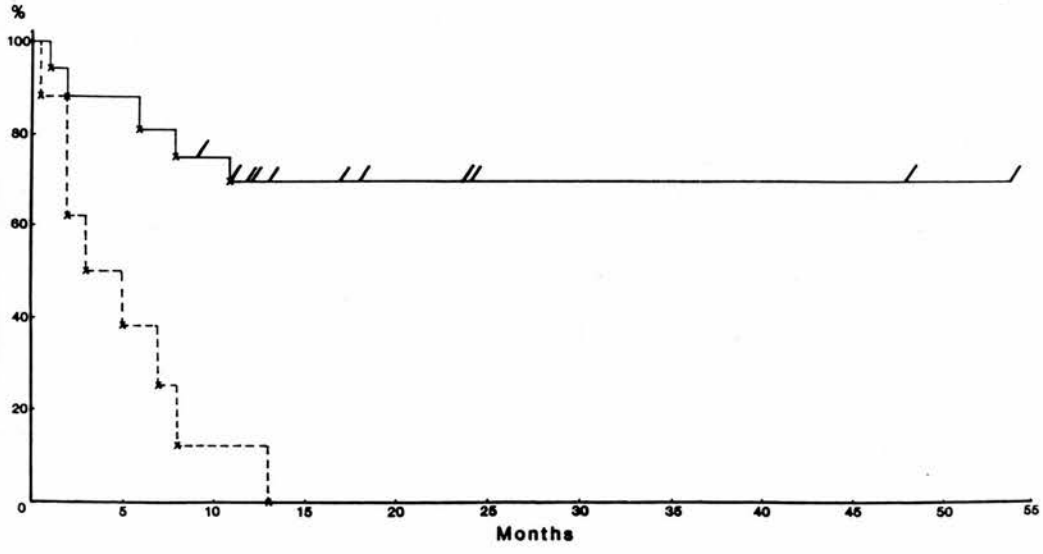



Fig 2. Disease free survival, first remission AML (——) versus others ( - - - - ) post ABMT.

The five patients treated in second remission have all relapsed and died (6, 7, 8, 9 and 14 months).

*Haematological recovery*

The mean dose of nucleated cells was $1{\cdot}85 \times 10^8$/kg (ABMT I and II included); range $0{\cdot}6$–$3{\cdot}1 \times 10^8$/kg.

Regeneration time after all ABMTs compared to contemporary patients allografted in our institution is shown in Table III.

Haematological recovery was delayed in the second ABMT (see Table IV) even though the mean dose of nucleated cells infused for each procedure was comparable.

*Morbidity*

*Infective complications.* There were 10 episodes of gram −ve septicaemia; four *Pseudomonas aeruginosa*, four *Escherichia coli*, one *Klebsiella aerogenes* and one *Flavobacterium* species. Seven patients had gram +ve organisms isolated from the blood, four of which were of doubtful significance.

14/24 had *Candida* species isolated from one or more sites. 21/24 patients with Hickman lines *in situ* had coagulase −ve staphylococci isolated from the entry site, 11/24 had diphtheroids isolated and only 3/24 had a *Staphylococcus aureus* isolated. However, only one patient was thought to have a septicaemia originating from the Hickman line (caused by a coagulase −ve staphylococcus).

**Table III.** Comparison of haematological recovery following ABMT I with contemporary allograft patients

| | Recovery in days following: | | |
|---|---|---|---|
| | | Autograft | |
| | Allograft ($n=10$) | A ($n=21$) | B ($n=24$) |
| Total WBC $>1000\times10^9$/l | 15 | 21 | 21 |
| Neutrophils $>500\times10^9$/l | 16 | 25 | 26 |
| Platelets $>50\times10^9$/l | 19 | 40 | 44 |

Day 0 = Day of AMBT. A = All patients autografted during remission. B = All patients whether autografted during remission or at relapse. Comparison of the difference between the means of each sample (for a small sample) showed no statistical difference.

**Table IV.** Comparison of haematological recovery in patients who received both ABMT I and II

| | Recovery in days following: | | |
|---|---|---|---|
| | ABMT I | ABMT II | |
| Total WBC $>1000\times10^9$/l | 18 | 26 | $P<0{\cdot}05$ |
| Neutrophils $>500\times10^9$/l | 21 | 30 | $P>0{\cdot}05$, $<0{\cdot}1$ NS |
| Platelets $>50\times10^9$/l | 27 | 42 | $P<0{\cdot}01$ |

$n=8$. Statistics are by Student $t$ test for paired samples.

*Non-infective complications.* One early death was from an intra-cerebral haemorrhage on day 12, before regeneration had occurred.

One patient with no past history of epilepsy had a grand mal convulsion for which there was no obvious explanation, on day 98 (day 24 post ABMT II) when the platelet count was $36\times10^9$/l, unsupported, and the total WBC and neutrophil count were 2·6 and $1{\cdot}1\times10^9$/l respectively. When the anti-convulsants were withdrawn 1 month later he suffered a further fit and has had to remain on medication.

All patients suffered from some degree of nausea and vomiting. The oldest patient in the series (57 years) failed to recover from this and at the time of relapse 7 months later had lost 22 kg.

## DISCUSSION

The first prerequisite for long survival in AML is the achievement of remission. Once this has been attained, treatment must be directed to maintaining this remission, although the optimal treatment modality to achieve this has not been defined. Conventional chemotherapy often given for extended periods of time only results in long-term survival rates of approximately 25% (Lister & Rohatiner, 1982). The option of an allogeneic graft is restricted to those young patients with a suitable HLA-matched donor, and the problems of GVHD, interstitial pneumonitis and immunosuppression cause considerable morbidity and mortality. The advent of T-cell depletion of donor marrow (Reisner *et al*, 1983; Prentice *et al*, 1982) may significantly reduce some of these difficulties, but there is little evidence as yet that it will enable allogeneic transplantation to be extended to the use of mis-matched family donors.

ABMT as rescue from high dose chemotherapy merits serious consideration as intensive consolidation therapy in first remission of adult patients with AML. The attractions of this approach are evident. Every patient has a donor; the immediate morbidity and mortality is very low compared to allogeneic transplantation and patients aged up to 57 years (UPN 41) have received this treatment. There is no GVHD and in our experience no interstitial pneumonitis.

The main disadvantage of using ABMT in leukaemia is the possibility that the graft is contaminated with leukaemia. Attempts are being made to 'purge' this residual leukaemia by drugs such as cyclophosphamide derivatives (Kaizer *et al*, 1981; Laporte *et al*, 1984) although the scientific basis for this is questionable. Furthermore, there is no proof that any sort of purging is required in this situation (Gorin *et al*, 1985). None the less, the basic idea behind our double autograft procedure is to both increase the cytoreductive effect and to effect an '*in vivo* purging'. This is based on the assumption that following marrow ablation normal cells regenerate more quickly than leukaemic cells and shortly after the first ABMT the ratio of normal to malignant cells will be greatest. Many patients cannot, however, tolerate two autografts.

This autograft series of ABMT in first remission differs from that of Burnett *et al* (1984), in that ablative chemotherapy rather than irradiation was used in an attempt to reduce morbidity and to allow two grafts to be carried out. There is no proven advantage yet to chemotherapy or TBI in this situation (Gorin *et al*, 1985). 11/16 (68·75%) of patients treated as consolidation therapy in first remission remain disease free with a median follow up of more than 16 months post ABMT (range 6–54 months). This is a small series of patients but these results are clearly encouraging. To date, all five relapses in first remission patients have occurred in patients who have received only one autograft, with a median disease free survival of 17 months, which is as good as other treatment regimens. None of the six patients who received both ABMT I and II have relapsed. This difference is not yet statistically significant but may mean that the second ABMT has resulted in a greater reduction of host disease. It could also mean that delay in haematological recovery after ABMT I which was the main reason for failing to proceed to ABMT II may be a characteristic of more aggressive or resistant disease and such patients may be a poor prognosis group, irrespective of whether they receive ABMT II or not.

Massive chemotherapy with ABMT rescue is also effective in inducing a CR in relapsed patients, but all eight of our relapsed and second remission patients have relapsed again within 13 months (2, 2, 3, 5, 7, 8 and 13 months) except for one patient who died on day 12 of an intra-cerebral haemorrhage. It is likely that this represents failure to eradicate disease in the patient rather than contamination of the cryopreserved marrow, although proof of this is still lacking.

The major practical difficulty of our double ABMT approach to treatment of patients with AML in first remission is the prolonged cytopenia which may follow particularly thrombocytopenia which has been the major cause of failure to proceed to ABMT II (see Table II), although no patient has required platelet support after discharge except for operative intervention. Autoantibodies have been identified in some patients following both autografts and allografts (Minchinton *et al*, 1984). We have identified a granulocyte autoantibody in one of our patients (UPN 128) who took 52 d to achieve a neutrophil count of $500 \times 10^9$/l; however, she was too thrombocytopenic to test for platelet autoantibodies. She achieved a platelet count of more than $100 \times 10^9$/l, day 494. Prolonged thrombocytopenia has also been reported post allograft (First *et al*, 1985), although the more prolonged and severe thrombocytopenia appears to be associated with the more severe grades of acute and chronic GVHD. The difference in incidence post allograft and autograft may also reflect previous chemotherapy damage to the infused autologous marrow.

In this series there has been no ABMT procedural deaths in first remission patients and this is of vital importance in the overall context of this therapy. However, most patients become pyrexial and septicaemia was documented in 41% of ABMT procedures.

The results of ABMT in first remission AML are encouraging and merit formal comparison with conventional therapy and allogeneic grafting in a large series of patients. In second remission results are disappointing and offer no advantage over conventional therapy.

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